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Postoperative Fatigue: Clinical Applications and Associated Influencing Factors

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Abstract: ***Postoperative fatigue (POF) refers to a widespread and common state of fatigue experienced by patients following surgery. It is typically characterized by symptoms such as weakness, lack of concentration, low mood, and sleep disturbances. This condition not only affects the patient's postoperative recovery but may also increase the length of hospital stays, delay functional recovery, and significantly reduce quality of life. The occurrence of postoperative fatigue is related to various factors, including the type of surgery, postoperative complications, preoperative health status, and the patient's personal characteristics (such as psychological state and underlying health conditions). Although postoperative fatigue is widely recognized in clinical settings, its specific mechanisms remain unclear. This article reviews the definition, epidemiological features, pathophysiological mechanisms, clinical manifestations, assessment methods, and clinical management strategies of postoperative fatigue. By analyzing relevant domestic and international literature, the article aims to provide clinicians with comprehensive management approaches for postoperative fatigue and discusses future research directions.***

Keywords: Postoperative fatigue, Influencing factors, Measurement tools, Treatment plans.

1. Introduction

Postoperative Fatigue (POF) refers to a persistent sense of fatigue experienced by patients after surgery, which cannot be alleviated by rest. This fatigue not only affects the patient's daily life but also prolongs recovery time and increases medical costs. In recent years, with continuous advancements in medical technology and the promotion of rapid rehabilitation concepts, clinical focus has shifted from solely the success of the surgery to the overall postoperative recovery process. Postoperative fatigue (POF) is a common complication following surgical procedures and has a significant impact on the patient's recovery process and quality of life. Studies have shown that most patients experience moderate to severe fatigue within the first week after surgery [1], with patients undergoing abdominal surgeries particularly affected [2]. The clinical manifestations primarily include a decrease in muscle strength, insomnia, difficulty concentrating, slow thinking, and are often accompanied by varying degrees of depressive symptoms [3]. While postoperative fatigue is common among all surgical patients, its severity and duration vary due to individual differences [4]. Therefore, investigating the factors influencing postoperative fatigue and developing effective interventions is crucial for improving patient outcomes.

2. Definition and Epidemiology of Postoperative Fatigue

The concept of postoperative fatigue was first introduced by Rose and King in 1978 [3]. It refers to a persistent sense of fatigue experienced by patients after surgery that cannot be relieved by rest. This fatigue not only affects the patient's daily life but also prolongs recovery time and increases medical costs. The epidemiological characteristics of postoperative fatigue show that its incidence varies across different types of surgeries. For example, the incidence of fatigue is higher in patients following heart surgery or major abdominal surgery, with fatigue often lasting up to one month [5]. In contrast, in uncomplicated gastrointestinal surgeries, fatigue can persist for up to three months. Smaller procedures, such as laparoscopic surgeries, tend to have a relatively lower incidence of fatigue [6]. Studies indicate that the incidence of postoperative fatigue ranges from 30% to 80%, depending on factors such as the type of surgery, patient age, and preoperative health status.

2.1 Incidence of Postoperative Fatigue

The incidence of postoperative fatigue varies significantly across different types of surgeries. Several studies have shown that the incidence of fatigue is particularly high among patients undergoing cancer surgeries. For example, a study on postoperative fatigue in breast cancer patients found that approximately 70% of patients experienced varying degrees of fatigue within one month after surgery [7]. Additionally, the incidence of postoperative fatigue is also high in cardiac surgery patients. Research indicates that about 60% to 80% of patients experience fatigue following coronary artery bypass grafting (CABG) surgery [8]. Compared to routine surgical procedures, cancer surgeries, which involve complex immune responses and prolonged treatment processes, typically have more significant and longer-lasting fatigue symptoms [9]. Furthermore, the incidence of postoperative fatigue is generally high after orthopedic, abdominal, and neurosurgical procedures, and it is closely related to postoperative complications, anesthetic dosage, and postoperative infections [10].

2.2 Impact of Postoperative Fatigue on Recovery

Postoperative fatigue is not merely a short-term symptom; it has long-term negative effects on the patient's overall recovery process. First, fatigue directly impacts the patient's ability to engage in activities and their quality of life. Many patients reduce physical activity due to excessive fatigue, which, in turn, affects the recovery of muscle strength and physical function. Studies have shown that postoperative fatigue is significantly correlated with adverse events during recovery, such as complications and prolonged hospital stays [9-10]. Furthermore, fatigue also has a negative impact on the patient's mental health. Many postoperative patients develop

anxiety, depression, and other psychological issues due to prolonged fatigue, which further hampers their recovery process [11].

The long-term presence of postoperative fatigue may also lead to the development of Chronic Fatigue Syndrome (CFS), a clinical syndrome characterized by persistent fatigue, often accompanied by symptoms such as sleep disturbances, difficulty concentrating, and reduced exercise tolerance. The onset of CFS not only increases the physical and psychological burden on patients but may also make it difficult for them to return to social and work life [12]. Therefore, managing postoperative fatigue is crucial for accelerating recovery and improving the patient's quality of life.

3. Pathophysiological Mechanisms of Postoperative Fatigue

The occurrence of postoperative fatigue is closely linked to complex biological mechanisms, involving changes in the immune system, neuroendocrine system, and metabolism. During surgery, the body undergoes significant physiological stress, activating multiple biological pathways that contribute to the development of fatigue. Below are the currently known primary biological mechanisms of postoperative fatigue, discussed in detail from the perspectives of immune response, neuroendocrine changes, and metabolic disturbances.

3.1 Immune Response

The immune system plays a crucial role in the development of postoperative fatigue. Surgical trauma and tissue damage activate the body's immune system, triggering a series of inflammatory responses. The release of inflammatory mediators is closely linked to the onset of fatigue symptoms. Studies have shown that many pro-inflammatory cytokines have been proven to induce fatigue after exogenous administration [13-14]. Even low levels of cytokines (which do not cause a rise in body temperature or other physical symptoms) can lead to a decrease in mood in healthy volunteers [15]. Surgical injury causes tissue damage, triggering both local and systemic inflammatory responses. The release of inflammatory mediators, such as cytokines (e.g., IL-1, IL-6, TNF-α), not only participates in tissue repair but also affects the central nervous system, contributing to the sensation of fatigue. Research indicates that cytokines (IL-1b and IL-6) can induce "sickness behavior" in humans, including fever, discomfort, pain, fatigue, low mood, and difficulty concentrating [15-17]. One study found a direct link between the activation of postoperative inflammatory responses and the intensification of fatigue [18-19]. Specifically, inflammatory factors activate inflammatory pathways in the central nervous system, affecting brain function and leading to fatigue. IL-6 and TNF-α are common inflammatory cytokines post-surgery. They not only play a role in immune responses but can also exacerbate fatigue through interactions with the brain-gut axis and the nervous system [20].

3.2 Neuroendocrine Changes

The neuroendocrine system is one of the key pathways in regulating postoperative fatigue. Physiological stress induced by surgery stimulates the activation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to an increase in the secretion of stress hormones such as cortisol. Cortisol helps the body cope with stress in the short term, but prolonged or excessive cortisol secretion can suppress normal immune function and potentially lead to fatigue and recovery difficulties [20-21].

Additionally, overactivation of the sympathetic nervous system is another important mechanism behind postoperative fatigue. Sympathetic activation triggers a series of physiological changes, including increased heart rate, elevated blood pressure, and metabolic changes. While these responses help with short-term physiological adaptation, they may lead to persistent fatigue in the long term. Research shows that increased sympathetic nervous activity in postoperative patients is closely linked to an intensification of fatigue [22].

Another significant neuroendocrine regulator is tryptophan. Tryptophan is the precursor to the neurotransmitter serotonin (5-HT), which is known to be involved in sleep and fatigue regulation. After surgery, the level of free tryptophan in the blood increases, which is associated with a higher amount of tryptophan entering the brain. This may lead to elevated 5-HT concentrations in certain areas of the brain, potentially increasing the need for sleep and contributing to central fatigue. A significant correlation has been observed between fatigue scores and plasma tryptophan levels [23]. This further exacerbates the patient's fatigue. Psychological factors, such as anxiety and depression, not only affect the patient's emotional state but also interact with the neuroendocrine and immune systems, intensifying the feeling of fatigue [24].

3.3 Metabolic Disturbances

Metabolic disturbances are also a significant biological mechanism behind postoperative fatigue. Acute metabolic changes after surgery are closely associated with systemic inflammatory responses, energy expenditure, and changes in metabolic products. During the postoperative recovery process, the body's energy demands increase sharply as tissue repair and immune responses require substantial energy, leading to an increased metabolic burden. Studies have found that postoperative patients often exhibit metabolic disturbances, such as glucose metabolism abnormalities and lipid metabolism disorders, which may exacerbate fatigue [25].

Research indicates that postoperative patients experience enhanced protein catabolism and reduced muscle protein synthesis, which may be one of the primary causes of postoperative fatigue. After abdominal surgery, reduced nutritional intake and loss of gastrointestinal function can partially explain why patients undergoing abdominal surgeries experience higher levels of postoperative fatigue compared to those undergoing orthopedic or middle-ear surgeries. However, simple fasting cannot explain the occurrence of postoperative fatigue, as healthy individuals undergoing fasting do not show the same decline in work capacity, skeletal muscle function, or increased fatigue after major surgeries. Furthermore, nutritional interventions alone

do not effectively reduce postoperative fatigue [26]. However, when the catabolic response to surgery is controlled by anabolic agents (such as human growth hormone) and nutritional support, improvements in overall muscle strength and lean tissue mass are associated with a reduction in postoperative fatigue [27-28]. Therefore, nutritional deficiencies partially, but not entirely, explain the etiology of postoperative fatigue. Additionally, changes in adipose tissue post-surgery may also be related to fatigue. Adipose tissue plays a regulatory role in the body through the secretion of adipokines (such as leptin and adiponectin), which are closely linked to energy balance and immune responses. Studies have found that elevated levels of leptin after surgery may exacerbate fatigue, while adiponectin, which is associated with energy expenditure and anti-inflammatory responses, may play a role in alleviating postoperative fatigue [29].

4. Clinical Manifestations of Postoperative Fatigue

Postoperative Fatigue (POF) is a multidimensional clinical symptom, typically characterized by persistent weakness, low mood, difficulty concentrating, and sleep disturbances. In severe cases, it can significantly affect the patient's recovery process and quality of life. The clinical manifestations of postoperative fatigue vary depending on individual differences, the type of surgery, and postoperative complications. Although the presentation of postoperative fatigue may differ, its common feature is the persistence of fatigue and its interference with daily functioning.

4.1 Major Clinical Symptoms of Fatigue

4.1.1 Weakness

Weakness is the most typical symptom of postoperative fatigue, manifested by a decrease in physical activity and a heightened sense of fatigue. Patients often report significant physical and energy depletion, and even simple daily activities (such as walking or climbing stairs) can lead to exhaustion [29].

4.1.2 Low Mood and Depressive Symptoms

Postoperative fatigue is often accompanied by low mood, anxiety, or depression. Patients may display mood swings or lose interest in their surroundings. Studies have shown that postoperative patients tend to experience more negative emotions due to the impact of fatigue, with some patients developing clinical depressive symptoms, which further exacerbate the feeling of fatigue [30,31].

4.1.3 Difficulty Concentrating

Postoperative fatigue also manifests as cognitive dysfunction. Patients frequently report feeling mentally sluggish and having difficulty concentrating. Postoperative fatigue can affect cognitive abilities, especially in patients undergoing more complex surgeries or those with extensive trauma. In such cases, postoperative cognitive impairments and fatigue often occur simultaneously [30,31].

4.1.4 Sleep Disturbances

Postoperative fatigue is closely related to a decline in sleep quality. Fatigued patients often report insomnia, difficulty falling asleep, or waking up during the night. Poor sleep further exacerbates daytime fatigue. Research indicates that the quality of sleep in postoperative patients is significantly correlated with the severity of fatigue [32].

5. Factors Influencing Postoperative Fatigue

Postoperative fatigue is a multifactorial symptom, and its clinical manifestations include not only weakness, cognitive impairments, low mood, and sleep issues, but are also influenced by various factors such as the type of surgery, postoperative complications, preoperative health status, recovery conditions, and psychological state.

5.1 Type of Surgery

The type of surgery plays a significant role in the incidence and severity of postoperative fatigue. Studies have shown that cancer-related surgeries (such as breast cancer and gastric cancer surgeries) are more likely to cause significant postoperative fatigue than routine surgical procedures. One study found that approximately 70% of breast cancer patients reported varying degrees of fatigue within one month after surgery [29]. Additionally, cardiac surgeries (such as coronary artery bypass grafting) are closely associated with postoperative fatigue, with about 60% to 80% of patients experiencing fatigue following surgery [24]. These surgeries typically involve longer durations of general anesthesia and greater physiological stress, which can significantly affect the patient's recovery.

5.2 Postoperative Complications

Postoperative complications are a significant factor influencing postoperative fatigue. Common complications such as postoperative infections, anemia, and malnutrition can exacerbate fatigue symptoms. For example, systemic inflammation caused by infectious complications can lead to disruption of the postoperative immune system, thereby intensifying the feeling of fatigue [28]. Additionally, postoperative anemia is closely related to fatigue symptoms. Anemia worsens the sense of weakness in patients, leading to delayed recovery [11].

5.3 Preoperative Health Status

The patient's preoperative health status also plays a critical role in the occurrence of postoperative fatigue. Patients with chronic conditions (such as diabetes and cardiovascular diseases) are at a higher risk of experiencing fatigue after surgery. Studies have shown that patients with poor physical fitness and multiple underlying health issues are more likely to experience significant fatigue symptoms postoperatively [7,9,11]. Additionally, age is another factor influencing postoperative fatigue. Elderly patients, due to a decline in immune function, tend to experience longer recovery times and more pronounced fatigue symptoms [25].

5.4 Postoperative Rehabilitation and Physical Activity

The level of physical activity after surgery is related to the

intensity of fatigue. A lack of sufficient physical activity, especially during the early rehabilitation phase, can lead to weakness and worsen fatigue symptoms. In contrast, appropriate postoperative exercise can significantly improve fatigue symptoms and aid in the recovery of physical function. Studies have shown that engaging in moderate aerobic exercise postoperatively can help reduce fatigue and promote recovery [23].

5.5 Psychological State and Emotions

Postoperative fatigue is also influenced by the patient's psychological state. Chronic fatigue is often accompanied by emotional disorders such as anxiety and depression. Research indicates that psychological stress and negative emotions can exacerbate the severity of postoperative fatigue [30]. One study found that patients who developed depressive symptoms after surgery experienced more severe and prolonged fatigue compared to those with stable emotional states. Therefore, psychological interventions are an important aspect of alleviating postoperative fatigue.

6. Measurement Tools for Postoperative Fatigue

Currently, there is no "gold standard" for assessing postoperative fatigue, which has limited the understanding of this condition. Initially, the Visual Analogue Scale (VAS) was used to measure postoperative fatigue. However, due to its inability to distinguish between physical and psychological fatigue, other scales such as the Profile of Mood States (POMS) and the Perioperative Fatigue Assessment Scale have since been developed. These scales can provide broad and accurate assessments of postoperative fatigue.

6.1 Visual Analogue Scale (VAS)

The Visual Analogue Scale (VAS) [31] was one of the earliest tools used to measure postoperative fatigue. Patients can mark their perceived level of fatigue on a scale based on their subjective feelings. With extensive research on postoperative fatigue, an improved version of the VAS has been developed, which is now applicable for assessing fatigue in patients following major surgeries [32]. The advantage of this scale lies in its simplicity and ease of understanding; however, its limitation is that it does not distinguish between fatigue caused by physical factors versus psychological factors. Therefore, it has certain limitations when evaluating postoperative fatigue.

6.2 Profile of Mood States (POMS)

The Profile of Mood States (POMS) was revised by domestic researchers such as Chi Songlin [33]. It is a multidimensional scale used to assess mood types, categorizing the subject's mood into six different dimensions: tension, depression, anger, fatigue, vigor, and confusion, with five items in each dimension [34]. This scale is widely used in the assessment of postoperative fatigue and has demonstrated high reliability and validity. However, since it is primarily designed to assess mood, it does not fully reflect the overall changes in fatigue before, during the early postoperative phase, and later stages. Therefore, it is important to combine this scale with others when evaluating the entire process of postoperative fatigue.

6.3 Perioperative Fatigue Assessment Scale (Identity-Consequence Fatigue Scale, ICFS)

The ICFS [35] was initially designed by Paddison and others as a self-assessment tool primarily used to measure fatigue during the perioperative period. It has undergone several revisions and validations and now consists of five dimensions — fatigue symptoms, fatigue outcomes, fatigue duration, fatigue causes, and management strategies — comprising a total of 31 items. The scale uses a five-point rating system, with positive items scored directly and reverse items scored in the opposite direction. The total score is the sum of the scores from all dimensions, with higher scores indicating greater fatigue. This scale has been shown to have good reliability and validity and plays a valuable role in evaluating postoperative fatigue.

7. Interventions and Treatment Strategies for Postoperative Fatigue

Postoperative fatigue is a common symptom that affects patients' postoperative recovery and quality of life. Despite its complex biological mechanisms, various intervention and treatment strategies have gradually been developed with further research. Treatment for postoperative fatigue typically includes pharmacological therapy, non-pharmacological therapy, and multidisciplinary management. In clinical practice, treatment plans often need to be tailored to the specific circumstances of the patient.

7.1 Pharmacological Treatment

Pharmacological treatment is one of the key methods for alleviating postoperative fatigue. Although there are currently no approved medications specifically for postoperative fatigue, several drugs have been used to alleviate its symptoms. The following are some commonly used classes of drugs:

7.1.1 Antidepressants

Postoperative fatigue is often accompanied by depressive symptoms, and antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), are commonly used to improve the patient's mood and reduce fatigue. Studies have shown that using SSRIs, such as sertraline, can improve both fatigue and depressive symptoms in postoperative patients [36]. Additionally, some studies have found that antidepressants can alleviate postoperative fatigue by improving sleep quality and increasing energy levels [37].

7.1.2 Analgesics

Postoperative pain is a significant factor contributing to fatigue, and appropriate pain management helps reduce pain, thereby indirectly alleviating fatigue. Research indicates that nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids can alleviate pain after surgery, thus reducing the occurrence of fatigue [36,38]. However, opioid use should be approached with caution to avoid dependence and side effects.

7.1.3 Immunomodulatory Drugs

Since immune responses are closely related to postoperative fatigue, some immunomodulatory drugs, such as anti-TNF-α antibodies, have been investigated for the treatment of postoperative fatigue. Although these drugs are still in clinical research stages, there is evidence suggesting that reducing postoperative inflammation may help alleviate fatigue [39].

7.2 Non-Pharmacological Treatment

Non-pharmacological treatments also play a crucial role in alleviating postoperative fatigue. Common non-pharmacological methods include exercise therapy, psychological interventions, and nutritional support.

7.2.1 Exercise Therapy

Moderate exercise helps strengthen physical capacity and alleviate fatigue symptoms. Studies have shown that engaging in appropriate aerobic exercises and strength training postoperatively helps promote recovery, improve sleep quality, and significantly reduce fatigue. Exercise can alleviate postoperative fatigue by improving cardiovascular function, enhancing blood circulation, and stimulating the release of endorphins. This is especially beneficial for cardiac surgery patients, as gradually increasing exercise intensity can noticeably reduce postoperative fatigue symptoms [40].

7.2.2 Psychological Interventions

Psychological interventions, such as cognitive behavioral therapy (CBT), meditation, and relaxation training, have gained increasing attention for their role in alleviating postoperative fatigue. Research has found that postoperative patients who undergo CBT can effectively reduce fatigue, improve mood, and enhance cognitive function. Meditation and relaxation training help reduce psychological stress, improve sleep quality, and alleviate fatigue symptoms [41,42].

7.2.3 Nutritional Support

Postoperative fatigue is closely associated with malnutrition, particularly deficiencies in nutrients such as protein, iron, and vitamin D. Appropriate nutritional interventions can improve the patient's physical condition and reduce fatigue. One study indicated that supplementing with a high-protein diet helps postoperative patients restore physical strength and reduce fatigue. Additionally, supplementing with antioxidants (such as vitamins C and E) has been found to help reduce fatigue caused by postoperative inflammation [42].

7.3 Multidisciplinary Management

Multidisciplinary management is an important trend in the treatment of postoperative fatigue, particularly in complex cases of postoperative fatigue. This management approach integrates the expertise of various disciplines, including surgery, psychology, sports medicine, and nutrition, to enhance treatment outcomes through a comprehensive approach.

7.3.1 Collaboration between Surgical and Anesthesia Teams

Surgeons and anesthesiologists play a foundational role in managing postoperative fatigue. Rational use of anesthetic drugs, postoperative pain control, and early rehabilitation exercises all help reduce the occurrence of postoperative fatigue. For example, studies have shown that low-dose anesthesia and early recovery activities can effectively reduce the incidence of postoperative fatigue [38].

7.3.2 Collaboration between Psychological and Rehabilitation Teams

Psychological and rehabilitation teams provide emotional support, cognitive behavioral therapy (CBT), and rehabilitation exercises. These interventions not only help improve the patient's mental state but also reduce postoperative fatigue by enhancing physical strength, alleviating pain, and improving sleep quality [43]. This team-based collaboration offers comprehensive intervention, thus improving the patient's quality of life after surgery.

7.3.3 Individualized Treatment Plans

Treatment for postoperative fatigue should be individualized according to the patient's specific circumstances. Factors such as the patient's age, type of surgery, complications, and psychological condition should be considered when developing a targeted treatment plan. For example, elderly patients may need more focus on pain management and psychological support, while younger patients may benefit more from exercise therapy and social support.

8. Summary

In summary, postoperative fatigue is a significant barrier to recovery after surgery. While progress has been made in the treatment of postoperative fatigue, its exact causes remain unclear, and there is still a lack of unified and effective treatment measures. Clinical trials on postoperative fatigue are relatively few, and they often focus on specific types of surgeries or patient populations, leading to insufficient diversity in research samples. This may reduce the applicability of results to a wider range of patients. Larger-scale, interdisciplinary clinical studies are needed to obtain more representative and universally applicable results. Although the immune, neuroendocrine, and metabolic mechanisms of postoperative fatigue have been studied to some extent, further research is required to explore the interactions between these mechanisms, particularly how modulating immune and neuroendocrine pathways can help alleviate fatigue. Western medicine primarily focuses on treatments such as recombinant growth hormones and nutritional support, while traditional Chinese medicine tends to use extracts from herbal materials to alleviate postoperative fatigue. Implementing appropriate and effective interventions targeting factors that may contribute to fatigue is crucial for improving the quality of life for postoperative patients.

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