

# *Research progress on risk factors of postoperative delirium in elderly patients with hip fracture*

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**Abstract:** Postoperative delirium (POD) is a common disease in elderly patients undergoing hip surgery. As we all know, age is a well-known risk factor. In this increasingly aging situation, the proportion of elderly patients undergoing surgery is increasing day by day. Among them, postoperative delirium is a common complication of hip surgery. It brings great physical and psychological damage to patients and leads to long-term cognitive dysfunction. Therefore, the occurrence of postoperative delirium and its perioperative related risk factors are still the focus of our research. Therefore, this review discusses the related risk factors of postoperative delirium in elderly patients undergoing hip surgery and summarizes the research progress of postoperative delirium in order to provide reference for related research.

## 1. Introduction

It is estimated that the global number of hip fractures will increase to 2.6 million in 2025 and 4.5 million in 2050<sup>[1]</sup>. The premature aging of the population may increase the absolute number of hip fractures<sup>[2]</sup>. Managing these fractures and changing prevention strategies will remain an important task for the global medical system. Hip fracture patients are usually elderly people with existing complications, including postoperative delirium and frequent multi-drug treatment<sup>[3]</sup>. At the same time, hip fracture also potentially leads to the loss of physical function, independence or death of patients<sup>[4]</sup>. Almost all patients need to undergo acute surgery, which increases the risk of surgical and medical complications<sup>[5]</sup>.

Hip replacement surgery is usually used for elderly patients with hip fracture or degenerative arthritis. Elderly patients undergoing hip replacement are at risk of occasional delirium, and about 20-50% of patients have delirium after hip surgery<sup>[6]</sup>. Old age, complications, bleeding during operation, anesthesia and hip surgery may be risk factors for postoperative delirium (POD), which are risk factors for decreased postoperative functional outcome, prolonged hospitalization and mortality<sup>[7]</sup>. Early identification of postoperative delirium (POD) is of practical clinical significance for improving the quality of life of elderly patients undergoing hip surgery.

## 2. Delirium

### 2.1 Definition

Post-operative delirium (POD) is an acute decline of attention and cognitive ability, which is a common, life-threatening and potentially preventable clinical syndrome in people aged 65 or above. Contrary to dementia, postoperative delirium, (POD) is an acute mental disorder<sup>[8]</sup>. Postoperative delirium (POD) is a very common and serious complication, especially in elderly inpatients, which often occurs within 1-3 days after operation, and the incidence rate is as high as 17%-61% in elderly patients undergoing complex and emergency surgery<sup>[9]</sup>.

Postoperative delirium often occurs in the elderly, which is the most common surgical complication in the elderly<sup>[10]</sup>. Hip replacement surgery is usually used for elderly patients with hip fracture or degenerative arthritis. Elderly patients undergoing hip replacement are at risk of occasional delirium. About 20-50% of patients have delirium after hip surgery<sup>[11]</sup>, and the incidence of delirium after hip fracture is as high as 50%<sup>[12]</sup>. It is reported that postoperative delirium (POD) may increase the incidence of postoperative complications and perioperative mortality. At the same time, postoperative delirium prolonged the hospitalization time and increased the hospitalization expenses, which brought long-term inconvenience to the elderly patients<sup>[11]</sup>. Although some risk factors of postoperative delirium have been clearly identified, including age, gender (male), history of chronic neurocognitive impairment or mental illness, and previous surgical history<sup>[13]</sup>. However, these risk factors cannot be changed and cannot be used as targets to prevent delirium. Therefore, the potential variable risk factors have become a hot issue in our current research.

### 2.2 Mechanism

As we all know, inflammation theory is a hot research theory at present, and the potential mechanisms of postoperative delirium include excessive release of inflammatory mediators, activation of glial cells, damage of blood-cerebrospinal fluid barrier, invasion of peripheral immune cells into central nervous system, and delayed recovery of postoperative inflammation<sup>[14]</sup>. Activation of microglia plays a key role in the disorder of central nervous system<sup>[15]</sup>. Microglia are resident immune cells in the central nervous system and highly mobile cells, which can promote synaptic activity and remodeling. Surgery causes inflammation, activates the innate immune system, and stimulates microglia activation. Overactivation of microglia will lead to damage to the central nervous system, thus reducing the threshold of postoperative delirium<sup>[16]</sup>. At the same time, the systemic inflammatory reaction after operation activates inflammatory mediators, which leads to the release of proinflammatory factors and destroys the blood-cerebrospinal fluid barrier. Toxins produced by bacteria pass through the blood-cerebrospinal fluid barrier and destroy the central nervous system function, which eventually leads to postoperative delirium<sup>[17]</sup>. The levels of some proinflammatory factors (such as TNF- $\alpha$ , IL-6, IL-8, IL-10 and C- reactive protein) in patients with postoperative delirium are higher than those in patients without postoperative delirium<sup>[18]</sup>. Generally speaking, there are two necessary conditions for postoperative delirium. One is that most of the people who have occurred are elderly people, because the physiological function of the elderly has deteriorated, and their compensation ability and ability to cope with stimuli have declined. The other is the stress stimulation of trauma, surgery, anesthesia, etc. which causes the changes of hormones and inflammatory factors in the body, which makes the imbalance between dopaminergic neurotransmitters and cholinergic neurotransmitters, thus triggering the delirium of patients.

### 3. Risk factors affecting postoperative delirium in elderly patients undergoing hip surgery.

Among many influencing factors, advanced age has been considered by most scholars as an independent risk factor for postoperative delirium. Including preoperative risk factors, intraoperative risk factors and postoperative risk factors. These include controllable factors and uncontrollable factors respectively<sup>[19]</sup>. Among these factors, age, sex, cognitive dysfunction (dementia, MMSE score screening cognitive function) and physical dysfunction, complications (diabetes, depression, anxiety, etc.), nutritional status and functional status (albumin, Katz score, vitamin D level), type of surgery (orthopedics, cardiovascular surgery, orthopedic surgery, emergency), type of surgery (hip fracture, anxiety, etc. The variable factors include the types of drugs taken by patients during perioperative period, inflammation, infection, perioperative pain, electrolyte disorder, perioperative blood transfusion, perioperative hemodynamic changes, anesthesia mode (general anesthesia/spinal anesthesia), anesthesia depth, intraoperative fluid replacement, etc.

A prospective study conducted by Vibeke<sup>[20]</sup> and others confirmed that pre-existing cognitive dysfunction, trauma and fever were independent risk factors for postoperative delirium in patients with hip fracture. Cristiana<sup>[21]</sup> and others also proved that aging and low functional reserve are also independent risk factors for postoperative delirium. Preoperative stroke history, preoperative surgical history, preoperative low oxygen saturation, preoperative poor sleep, excessive use of fentanyl and other anesthetic drugs, blood transfusion and infection have all proved to be independent risk factors for postoperative delirium<sup>[22]</sup>. At present, vitamin D deficiency is considered to be a worldwide problem. Due to age-related exposure to sunlight and insufficient intake of dietary vitamin D, the elderly are particularly prone to vitamin D deficiency. Many studies have reported the correlation between low vitamin D level and cognitive impairment<sup>[23-25]</sup>. In addition to maintaining calcium and phosphorus homeostasis, vitamin D can also protect the brain from cognitive damage by preventing cardiovascular disease. Some related studies have pointed out that there is a dose correlation between serum 25-OH-D concentration and cognitive function, but the relationship between serum 25-OH-D concentration and cognitive function in current research is not clear<sup>[25]</sup>.

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## 4. Prevention and treatment of postoperative delirium in elderly patients undergoing hip surgery

### 4.1 Evaluation method

Early diagnosis and treatment with delirium assessment tools before operation is an important measure to improve the perioperative prognosis of elderly patients. In our clinical work, we should evaluate the elderly patients over 65 years old before operation, screen out the risk factors before operation, and carry out better clinical intervention during perioperative period to minimize the occurrence of postoperative delirium. In the past, most domestic studies often used Delirium Scale (CAM) and Mini-mental State Examination (MMSE) to evaluate the postoperative cognitive function of patients<sup>[35]</sup>. There is also a cognitive impairment assessment after surgery using the Montel Cognitive Function Assessment Scale (MoCa), which was developed by Professor Nasreddine<sup>[36]</sup> in 2004. It is an assessment tool for rapid screening of Mild Cognitive Impairment, MCI). The cognitive areas of assessment include attention and concentration, executive function, memory, language, visual structure skills, abstract thinking, calculation and orientation. As far as possible, the standardized scale will be used to identify the early evaluation, and various evaluation scales will be applied to clinical work practice to provide convenience for our clinical work.

### 4.2 Preventive intervention measures

Medical staff should comprehensively evaluate the overall situation of patients from the initial stage of hospitalization, formulate different diagnosis and treatment plans according to different conditions, and give symptomatic treatment quickly. This greatly reduces patients' negative emotions and improves patients' hospitalization experience. It is very important to relieve patients' pain before operation. Most orthopedic patients take pain as the main symptom, and elderly patients are often unbearable because of pain, which seriously affects patients' mood and sleep quality, and even causes mental symptoms. Postoperative pain is also an important influencing factor. Lynch et al.<sup>[37]</sup> collected data of 477 patients undergoing elective non-cardiac surgery to explore the relationship between postoperative pain and delirium, and found that the higher the static pain score, the greater the risk of delirium. A prospective study found that moderate and severe pain and the increase of baseline pain on the first day after operation were independent predictive risk factors for postoperative delirium<sup>[38]</sup>.

Patients are prone to postoperative delirium because of surgical trauma and other reasons, especially the elderly. For these patients, the first thing is necessary psychological counseling, necessary explanations for incision pain and oozing blood, and efforts to eliminate patients' nervous negative emotions. This can greatly reduce the postoperative anxiety of patients and reduce the incidence of postoperative delirium as much as possible. Clear postoperative rehabilitation goals, effective monitoring of patients' blood sugar, timely control of patients' blood sugar through insulin. Perioperative anemia should be corrected by autologous blood transfusion and preoperative blood transfusion, and moderate and severe anemia should be corrected before operation<sup>[39]</sup>. Diet should be given a high-protein, digestible diet, keep the stool unobstructed, and correct hypoproteinemia in time<sup>[40]</sup>. Multi-mode analgesia and preemptive analgesia were used to ensure patients' rest and sleep. These nursing measures can effectively reduce the occurrence of postoperative delirium.

## 5. Summary

We identify the risk factors related to postoperative delirium in elderly patients undergoing hip surgery during perioperative period, and provide predictive value for postoperative delirium. Postoperative delirium, as a postoperative nervous system disease, leads to cognitive dysfunction and

long-term poor functional outcome in elderly patients. Therefore, based on the current risk factors, we can formulate a series of clinical interventions and preventive measures to significantly reduce the incidence of postoperative delirium. Novel coronavirus's (COVID-19) in recent two years, as a respiratory disease, seriously affects the survival rate and quality of life of patients. It is reported that COVID-19 is a new risk factor for postoperative delirium (POD)<sup>[41]</sup>. Therefore, further clinical research is needed in the future research to clarify the relationship between novel coronavirus's patients and postoperative delirium, which will become a new trend in the future.

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