Article

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Exploring the Potential Role of Dexmedetomidine in Reducing Postoperative Cognitive Dysfunction in Elderly Hip Fracture Patients

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Abstract

Background: Hip fractures are prevalent in the elderly; however, Postoperative Cognitive Dysfunction (POCD) is a possible complication of hip fracture surgery in elderly patients. This study examines the influence and the underlying mechanism of dexmedetomidine on POCD in elderly patients following hip fracture surgery.

Methods: The retrospective study involved elderly patients with hip fracture who were treated at the Fifth Affiliated Hospital of Xinjiang Medical University from October 2021 to August 2022. During the surgery procedures, dexmedetomidine was administrated and the peripheral blood samples were collected from the patients. Inflammatory factors were measured using Enzyme-linked immunosorbent assay (ELISA), while pyroptosis-related proteins were detected through quantitative reverse transcription PCR (RT-qPCR) and western blot. Additionally, the levels of CD4+T and CD8+T cells were assessed using flow cytometry. An aged rats hip fracture model was established to further investigate the impact of dexmedetomidine on postoperative mobility, cognition function, pyroptosis and immune cells in rats.

Results: Postoperative cognitive function in patients did not show significant alteration when compared with preoperation levels ($p > 0.05$). There were notable reduction in the levels of interleukin-18 (IL-18), Caspase-3, Gasdermin-D (GSDMD) and NLR Family Pyrin Domain Containing 3 (NLRP3) ($p < 0.001$), accompanied by an increase in the proportion of CD4+T cells and an decrease in CD8+T cells after operation ($p < 0.01$). In aged rats, postoperative exploratory activities increased compared to their preoperative state. Compared with preoperative levels, the levels of interleukin-1β (IL-1β), IL-18, Caspase-3, GSDMD, and NLRP3 were significantly decreased ($p < 0.001$), the proportion of CD4+T cells was increased, and the proportion of CD8+T cells was decreased postoperatively ($p < 0.01$).

Conclusions: Although there was no significant alteration in postoperative cognitive function in patients, dexmedetomidine may still play a role in mitigating POCD potentially due to its effects on reducing immune inflammation and pyroptosis markers. Further research is needed to fully understand the underlying mechanisms and its clinical implications.

Keywords

senile hip fracture; cognitive dysfunction; dexmedetomidine; pyroptosis

Introduction

Hip fractures frequently occur in the elderly, necessitating surgery as a common treatment option [1]. Postoperative Cognitive Dysfunction (POCD) may arise as a complication following hip fracture surgery in elderly patients [2]. Cognitive dysfunction following hip fracture surgery in the elderly has a negative impact on the rehabilitation and quality of life, while also amplifying the burden on both the patients and their families [3]. Cognitive dysfunction after hip fracture surgery in the elderly, including delirium and/or dementia, will make the treatment and recovery of hip fracture more complicated [4]. Consequently, it is necessary to devote sufficient attention to implementing comprehensive treatment strategies to improve the cognitive function and quality of life for the elderly.

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Cognitive dysfunction may be associated with a variety of factors, such as immune inflammation and pyroptosis [5]. Hip fracture surgery may trigger a systemic inflammatory response and also provoke neuroinflammation in the brain. Neuroinflammation can result in nerve cell damage through mechanisms like apoptosis, necrosis and pyroptosis, which may contribute to the development of POCD [6]. Pyroptosis is a form of programmed cell death between apoptosis and necrosis. It usually plays an important role in inflammation and immune response. This process can result in the leakage of intracellular contents, thereby exacerbating the inflammatory response [7,8].

The severity and recovery rate of cognitive dysfunction after hip fracture surgery in the elderly are influenced by multiple factors, including the type of surgery, anesthetics, postoperative complications, the patient's physical condition, nutritional status and mental state [9]. Among various strategies, optimizing the anesthesia protocol to minimize the risk of cognitive dysfunction is currently a critical challenge. Dexmedetomidine (DEX), an α2-adrenoceptor agonist, is known for its sedative, anxiolytic, analgesic and stress-reducing effects [10]. Research indicates that patients administrated dexmedetomidine during anesthesia are less likely to develop POCD [11,12]. Furthermore, dexmedetomidine also has anti-inflammatory effect [13]. While studies on the link between dexmedetomidine and pyroptosis in POCD in the elderly are still scarce, this study seeks to explore the protective effect of dexmedetomidine on postoperative cognitive function and the underlying mechanisms in elderly patients undergoing hip fracture surgery. This study aims to elucidate the protective mechanism of dexmedetomidine, offering new novel insights and therapeutic targets for clinical practice.

Materials and Methods

Case Selection

This investigation involved ten patients aged over 74 years, who underwent prosthesis replacement or open reduction and internal fixation for hip fractures in the Fifth Affiliated Hospital of Xinjiang Medical University from October 2021 to August 2022. The right upper limb vein was routinely cannulated in all patients, and vital signs such as blood pressure, heart rate, and blood oxygen saturation were monitored to ensure the safety of anesthesia. Dexmedetomidine was administrated to the patients during the operation, and the dose and speed were adjusted according to the patient's weight and anesthesia requirements. Peripheral blood samples were collected 24 hours before operation and 48 hours after operation, and Minimental State Examination (MMSE) [14] was performed before operation, 24 hours and 48 hours after operation. The study was approved by the Medical Ethics Committee of the Fifth Affiliated Hospital of Xinjiang Medical University (XYDWFYLSH-2021-024) and followed the Helsinki Declaration. Patients were informed and signed the consent form before surgery. This study was also approved by the Animal Ethics Committee, with the ethical approval number: IACUC-20210530-67.

Inclusion criteria: (1) no drugs affecting cognition were used before surgery; (2) the preoperative MMSE scores were more than 24 points; (3) no serious respiratory disease, no serious cardiovascular and cerebrovascular disease (systolic blood pressure was not higher than 160 mmHg, diastolic blood pressure was not higher than 90 mmHg in patients with hypertension after medical treatment). Exclusion criteria: (1) patients with severe liver and kidney dysfunction (aspartate aminotransferase/alanine aminotransferase more than 1.5 times the upper limit of normal, creatinine/urea nitrogen more than the upper limit of normal); (2) taking sedatives for a long time and having a history of abnormal recovery from anesthesia and surgery; (3) patients with preoperative mental and nervous system diseases, unexpected bleeding during operation, and significantly prolonged operation time; (4) patients with severe drug allergy or other reasons were difficult to cooperate.

At the conclusion of the experiment, the experimental rats were treated according to ethical guidelines. If euthanasia was required, it was performed using a humane method involving anesthesia followed by cervical dislocation or carbon dioxide (CO_2) inhalation. If euthanasia was not required, the rats were kept in the laboratory under normal conditions for further observation.

ELISA Detection

The serum concentrations of inflammatory markers, specifically interleukin-1β (IL-1β) and interleukin-18 (IL-18), were quantitated using Enzyme-linked immunosorbent assay (ELISA). The assay was conducted in accordance with the manufactory protocols for the IL-1β ELISA kit (Jianglai Biological, JL13662, China) and IL-18 ELISA kit (Jianglai Biological, JL19261), The absorbance was measured at OD450. The variations in the inflammatory factors levels before and after surgery were determined.

Establishment of Rat Hip Fracture Model

Twelve Sprague Dawley (SD) rats (18–24 months old, 450 g ± 20 g) purchased from the Animal Experiment Center of Xinjiang Medical University were adaptively housed to mitigate manipulative stress. The rats were randomly divided into four groups: control group (NC, N = 3), model group (N = 3), model + normal saline group (N = 3), model + dexmedetomidine group (N = 3). 3% pentobarbital sodium was injected intraperitoneally at a dose of 50 mg/kg to anesthetize rats. The rats were positioned on the operating table, their limbs were secured, the fur at the surgical site was shaved, and the skin was sterilized. The surgical area was exposed by covering the surrounding area with a sterile surgical towel. A skin incision was then carefully made along the posterior side of the rat's hip joint to isolate the subcutaneous tissue and expose the hip joint. In the model group, near the hip joint, locate the proximal femur. Apply gentle pressure to the proximal part of the femur using forceps to break it. Sew the separated tissue layer by layer and close the skin. Return the rats to their rearing cage and ensure the animals have access to enough food and water. Among the 12 SD rats, 3 rats in the model + normal saline group were intraperitoneally injected with normal saline during the operation, and 3 rats in the model + dexmedetomidine group were intraperitoneally injected with dexmedetomidine at 30 μg/kg during the operation. The injections were administered immediately during the fracture surgery. Both normal saline and dexmedetomidine were given at the time of surgery to evaluate their effects postoperatively. X-ray films were captured 6 weeks after the After surgery. The hippocampal tissue was collected using the following procedure: the rats were anesthetized intraperitoneally with 3% pentobarbital sodium at the dose of 150 mg/kg and then the brains were promptly decapitated. The hippocampus was rapidly harvested and dissected on an ice plate, rinsed with precooled saline, and placed in Eppendorf (EP) tubes. Subsequently, the tissue was frozen in liquid nitrogen and ultimately stored in a –80 °C freezer. Rat tail blood was collected by fixing the animal for 5 to 10 mm, then massaging the tail from the root to the tip, allowing the blood to flow from the tip of the tail.

Y-Maze and Mine Field Experiments to Detect Animal Behavior

In the Y maze experiment, each channel of Y maze is 45 cm in length, 14 cm in width and 15 cm in height. The center area is composed of an equilateral triangle with 14 cm in length. The top of the maze is covered with a transparent cover and the ambient light is kept dark during the experiment. To familiarize the animals with the experimental environment, they were placed in the starting channel of the Y maze and allowed to explore freely. Seal one of the lanes and allow the animal to start from the starting lane and explore the remaining two lanes. After 3 minutes, the animal was removed from the maze. The entrance to the new channel was opened and removed 3 minutes after each rat entered from the starting channel for 5 minutes each test. The proportion of rats entering the new channel, the total distance and the total exercise time were recorded [15].

Table 1. Primer sequences.

Genes	Primer sequence
Human *caspase-3*	F: 5′-GCGGATGGGTGCTATTGTGAGG-3′
	R: 5′-GCCACGGATACACAGCCACAG-3′
Human *NLRP3*	F: 5′-AGGGATGAGAGTGTTGTGTGAAACG-3′
	R: 5′-GCTTCTGGTTGCTGCTGAGGAC-3′
Human *GSDMD*	F: 5′-GCTGACCTCTGCCCTCCTTC-3′
	R: 5′-TGGTGTGTGCGTTGGAATGC-3′
Human *β-actin*	F: 5′-GCCTCGCCTTTGCCGAT-3′
	R: 5′-AGGTAGTCAGTCAGGTCCCG-3′
Rat *caspase-3*	F: 5′-TGACTGGAAAGCCGAAACTC-3′
	R: 5′-AGCCTCCACCGGTATCTTCT-3′
Rat *NLRP3*	F: 5′-TGCATGCCGTATCTGGTTGT-3′
	R: 5′-ACCTCTTGCGAGGGTCTTTG-3′
Rat *GSDMD*	F: 5′-GCAACTTCCAAGTCTCCGATGTC-3′
	R: 5′-CTGAGTCACACGCAGCATACAC-3′
Rat *β-actin*	F: 5′-CACCCGCGAGTACAACCTTC-3′
	R: 5′-GTACATGGCTGGGGTGTTGA-3′

NLRP3, NLR Family Pyrin Domain Containing 3; *GSDMD*, Gasdermin-D.

For the model group and the model + saline group, no anesthesia was used during these behavioral tests to ensure that the animals' natural exploratory behavior was observed.

In the Mine experiment, the open box of mine experiment was 80 cm in length and width and 30 cm in height, and the bottom was composed of 16 squares with equal area (20 cm × 20 cm). The ambient light was maintained at a low level throughout the experiment to simulate a dim environment. Initially, acclimate the animals to the experimental environment by placing them in the center of the platform and allowing them to explore freely. Before the formal experiment, each rat was allowed to explore the platform for 2 minutes to acclimate to the environment and then was removed from the platform. During each rat replacement, feces and urine were wiped off with a tissue, followed by cleaning the chamber with alcohol to eliminate the scent of the previous rat. During the experiment, each rat was tested once, and each test lasted for 5 minutes. The proportion of movement distance in the central area, the total movement distance and the time to enter the central area of the rats were recorded.

RT-qPCR

Total RNA was extracted from blood and hippocampus using TRIzol reagent (manufacturer: Thermo Fisher Scientific; Waltham, MA, USA). The RNA concentration and quality were determined following centrifugation and washing to remove impurities. The extracted total RNA was subjected to a reverse transcription reaction using a reverse transcription kit (manufacturer: Thermo Fisher Scientific; Waltham, MA, USA) to generate cDNA. The cDNA samples were used in the real-time quantitative PCR (qPCR) reaction. Reaction conditions were as follows: 95 °C for 10 minutes; 40 cycles at 94 °C for 10 seconds; At 65 °C for 20 seconds; At 72 °C for 60 seconds; And 10 minutes at 72 °C. Primer sequences are listed in Table 1. The experimental data were analyzed, and the relative quantitative analysis was performed by the $2^{-\Delta\Delta Ct}$ method using the internal control gene *β-actin*.

Western Blot

Protein extraction was performed by cleaving blood or hippocampal tissue on ice with Radioimmunoprecipitation Assay Buffer (RIPA) buffer, and protein concentrations were subsequently determined. Equal amounts of protein samples were mixed with Sodium Dodecyl Sulfate Polyacrylamide Gel Electrophoresis (SDS-PAGE) loading buffer and treated with heat to 95–100 °C for 5 minutes. The samples were loaded onto a polyacrylamide gel for electrophoresis to separate the proteins along the gel. The proteins in the gel were transferred to a Polyvinylidene Difluoride Nitrocellulose (PVDF NC) membrane using a wet method. Nonspecific binding sites on the membrane were blocked with 5% skim milk or Bovine Serum Albumin (BSA) and incubated for 1 hour at room temperature. The membranes were subsequently incubated with specific Caspase-3 (ABclonal [Woburn, MA, USA], A25309, 1:2000), Gasdermin-D (GSDMD) (ABclonal, A20728, 1:2000), NLR Family Pyrin Domain Containing 3 (NLRP3) (ABclonal, A5652, 1:2000), and β-actin (ABclonal, AC026, 1:2000) antibodies at 4 °C overnight. The membranes were then incubated with the corresponding secondary antibodies (ABclonal, A23074, 1:5000) for 1–2 h at room temperature. Chemiluminescence substrates were used to detect protein signals on the membrane, and images of protein bands were acquired by exposure imaging systems (ChemiDoc, Bio-rad, Hercules, CA, USA). The gray value of protein bands was quantified by ImageJ analysis software (v1.8.0.345, National Institutes of Health, Bethesda, MD, USA) to evaluate the expression of the proteins.

Flow Cytometry

Ethylenediaminetetraacetic Acid (EDTA) anticoagulant was added to the blood sample, and mononuclear cells were isolated from the blood by Ficoll gradient centrifugation. Aliquots of cell suspension (2×10^6 cells/tube) were prepared for each tube. Cells were incubated with fluorescently labeled antibodies for 30 min before flow cytometry analysis. The collected data were analyzed using FlowJo flow cytometry analysis software. FITC-conjugated anti-CD45 antibody (BioLegend, San Diego, CA, 384405, USA), PE-conjugated anti-CD4 antibody (BioLegend, San Diego, CA, 980804, USA), FITC-conjugated anti-CD3 antibody (BioLegend, 317306, USA) and PE/Cyanine7-conjugated anti-CD8 (BioLegend, 300913, USA) antibody were used to detect the levels of CD4+T cells and CD8+T cells in human blood. FITC-conjugated anti-CD3 antibody (BioLegend, 201403, USA), PC7-conjugated anti-CD8 antibody (BioLegend, 201715, USA), and PE-conjugated anti-CD4 antibody (BioLegend, 203307, USA) were used to detect the levels of CD4+T cells and CD8+T cells in rat blood.

Statistical Analysis

GraphPad Prism (GraphPad Software Inc., version 9.0.0, San Diego, CA, USA) was used for data analysis. For clinical data involving repeated measurements, the first step is to conduct a sphericity test. If the data passes the sphericity test, repeated measures analysis of variance (ANOVA) is used. For animal data, the first step is to perform a Shapiro-Wilk test to determine if the data follows a normal distribution. If the data is normally distributed, *t*-tests and one-way ANOVA are employed. If the data is not normally distributed, rank-sum tests and Kruskal-Wallis H test are used. Data were presented as mean ± SD. p-value < 0.05 was considered statistically significant.

Results

MMSE Scores of the Patients

When accessing the patients' cognitive ability, it was observed that the MMSE scores exhibited a tendency to increase 24 h and 48 h post-surgery. This trend did not reach the statistical significance (Table 2, $p > 0.05$), possible due to the small sample size.

Table 2. MMSE scores of the patients (n = 10).

	Preoperative	24 hours after surgery	48 hours after surgery
MMSE	24	25	25
	25	26	26
	24	26	26
	24	27	27
	24	24	24
	25	24	24
	23	25	26
	24	25	25
	24	24	24
	25	24	24
Mean ± SD	24.20 ± 0.63	25.00 ± 1.05	25.10 ± 1.10
Mean ± SD of difference		–0.80 ± 1.32	–0.90 ± 1.45
Mauchly's test of sphericity		$p = 0.754$	
F-value		4.541[a]	
p-value	Reference	0.120	0.083

[a] Accurate statistics. MMSE, Mini-mental State Examination.

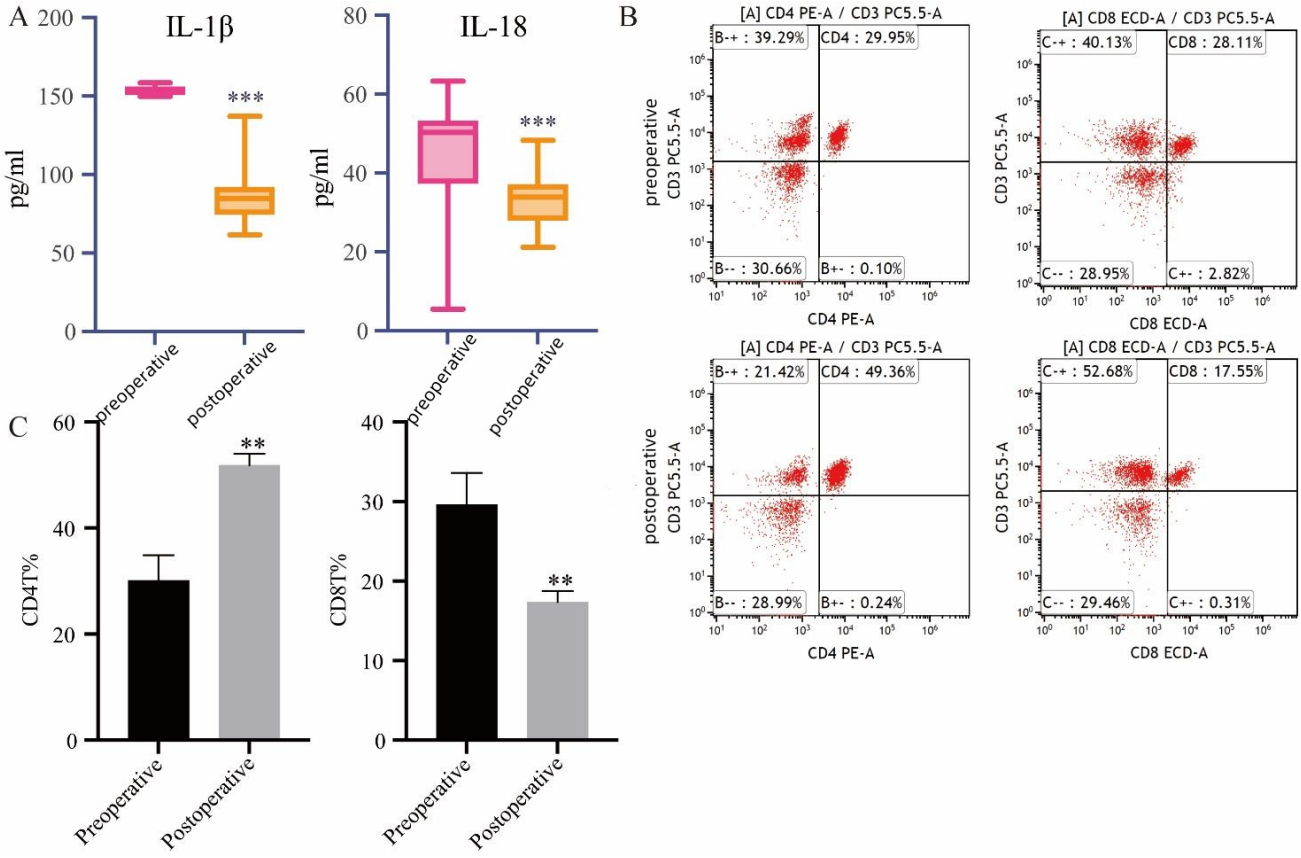

Fig. 1. Preoperative and postoperative immune-inflammatory changes in elderly patients with hip fracture (n = 10). (A) Changes in the expression of inflammatory factors before and after hip fracture surgery in the elderly were statistically significant. ***$p < 0.001$. (B) Flow cytometry was used to detect the levels of CD4+T cells and CD8+T cells before and after hip fracture surgery in the elderly. (C) Statistical results of the ratio of CD4+T cells and CD8+T cells. **$p < 0.01$. IL-1β, interleukin-1β; IL-18, interleukin-18.

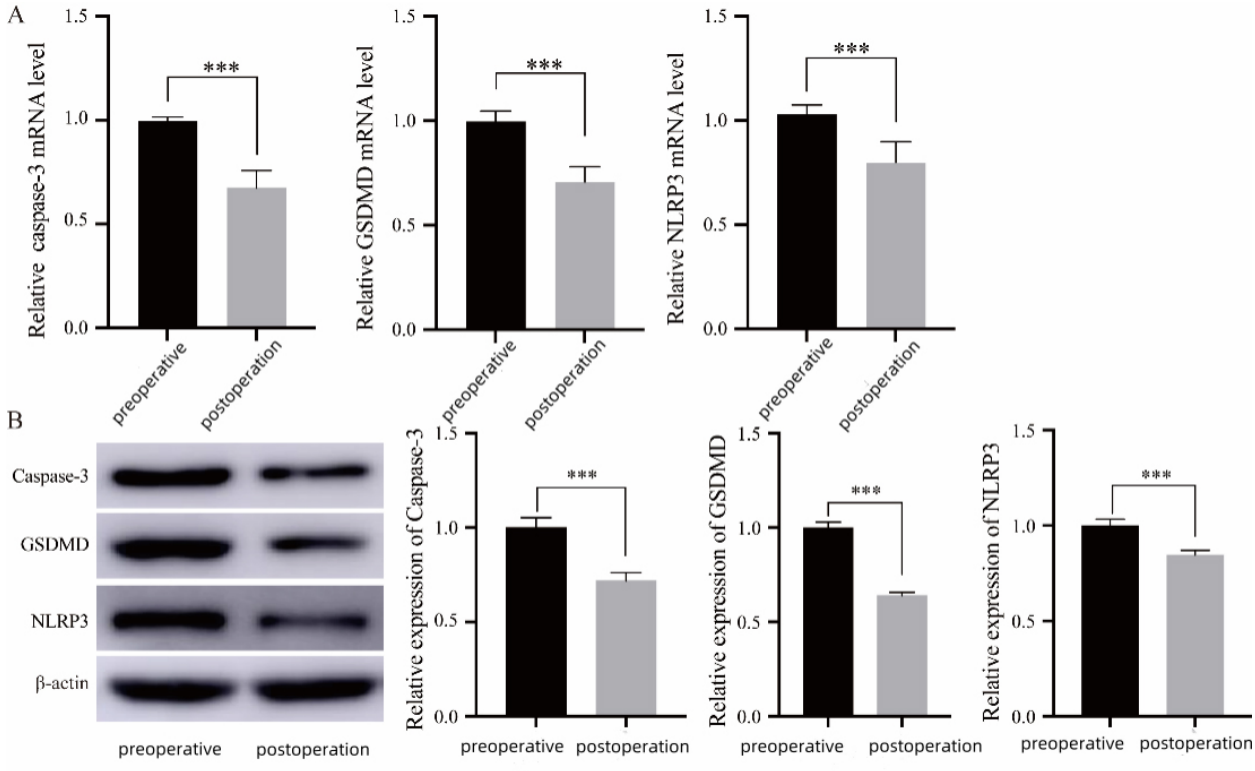

Fig. 2. Detection of pyroptosis-related protein expression before and after hip fracture surgery in the elderly (n = 10). (A) Quantitative reverse transcription PCR (RT-qPCR) was used to measure mRNA levels of Caspase-3, GSDMD, and NLRP3. (B) Western blot was used to detect the protein expression levels of Caspase-3, GSDMD and NLRP3. ***$p < 0.001$.

Changes of Immune Cells and Pyroptosis after Hip Fracture Surgery in the Elderly

IL-1β and IL-18 were significantly decreased after hip fracture surgery (24 h) in the elderly compared with that pre-surgery ($p < 0.001$), as shown in Fig. 1A. This decrease may be related to the administration of dexmedetomidine during surgery, which has known anti-inflammatory properties. The levels of peripheral blood CD4+T cells in postoperative patients (24 h) increased while CD8+T cells decreased as compared with those pre-surgery ($p < 0.01$), as shown in Fig. 1B,C.

The expression levels of Caspase-3, GSDMD and NLRP3 in the peripheral blood of the patients were detected by quantitative reverse transcription PCR (RT-qPCR) and western blot. The results showed that the mRNA and protein levels of these pyroptosis-related genes were significantly reduced after surgery compared with those before surgery ($p < 0.001$), as shown in Fig. 2.

Dexmedetomidine Alleviates Postoperative Cognitive Dysfunction in Rats with Hip Fracture

X-ray results confirmed fracture of the hip in the fracture model: the proportion of bone formation area increased, and some fracture lines existed, as shown in Fig. 3A. The behavioral examination showed that the rats had reduced movements and no exploration consciousness after fracture. However, the postoperative rats that received dexmedetomidine anesthesia had increased exploratory movements, suggesting that dexmedetomidine may have improved the postoperative motor and cognitive functions of the rats ($p < 0.05$), as shown in Fig. 3B,C.

Dexmedetomidine Inhibits Pyroptosis in Rats with Hip Fracture

Compared with the control group, the levels of Caspase-3, GSDMD and NLRP3 in the elderly rat hip fracture model group were significantly increased ($p < 0.001$) as shown in Fig. 4, while Caspase-3, GSDMD and NLRP3 levels were significantly decreased in the rats anesthetized with dexmedetomidine during the operation ($p < 0.001$), as shown in Fig. 4.

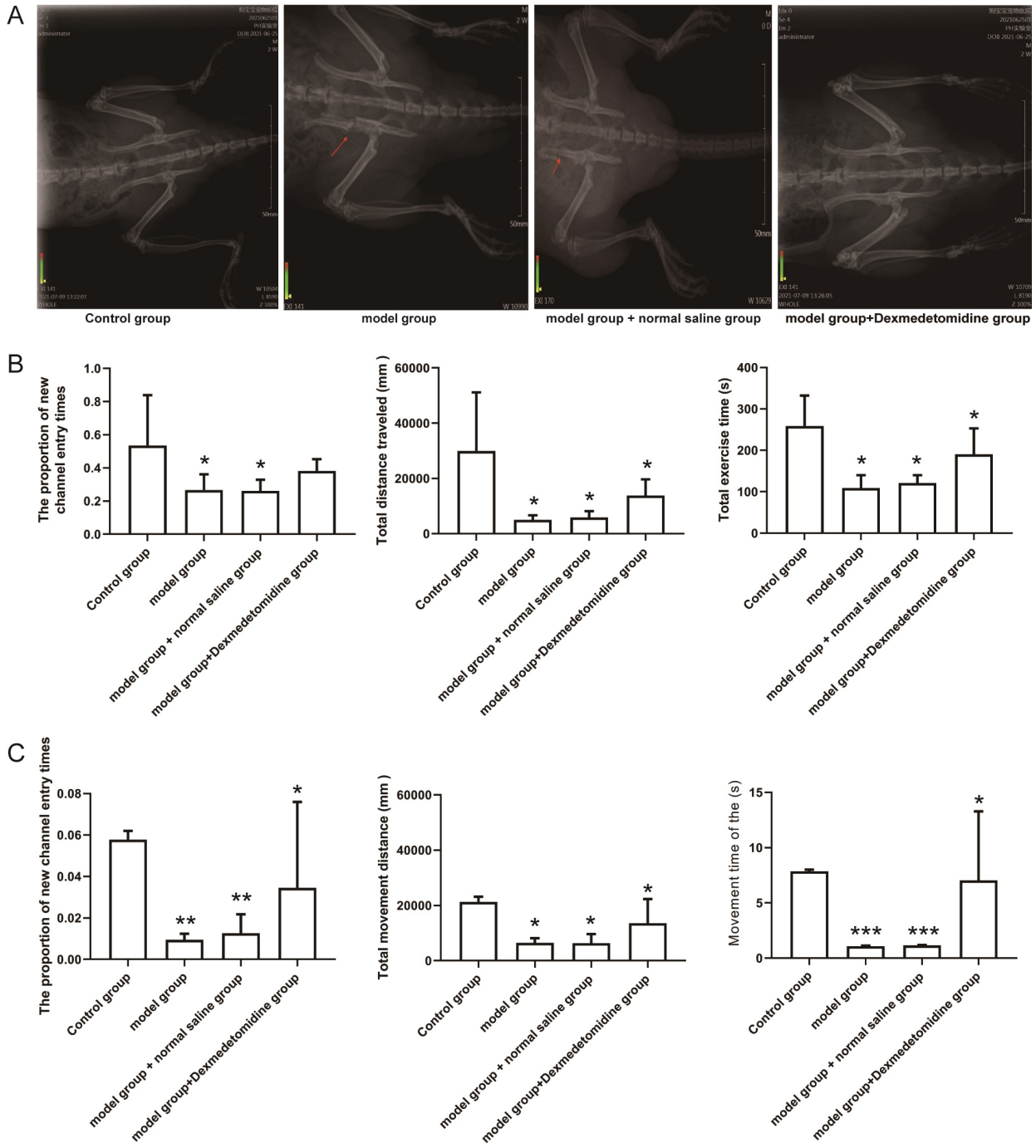

Fig. 3. Behavioral measurements of rats before and after hip fracture surgery (n = 12). (A) X-rays of rats in each group. (B) Y-maze test of rats in each group. (C) Mine field experiments of rats in each group. The arrow points to the fracture line. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Dexmedetomidine Increases the Proportion of CD4+T Cells after Hip Fracture in Rats

The level of CD4+T cells was decreased in the model group, while the level of CD4+T cells was increased in the rats anesthetized with dexmedetomidine during the operation ($p < 0.05$). CD8+T cells were significantly increased in the model group compared to the control group and decreased in the rats anesthetized with dexmedetomidine during surgery ($p < 0.01$), as shown in Fig. 5.

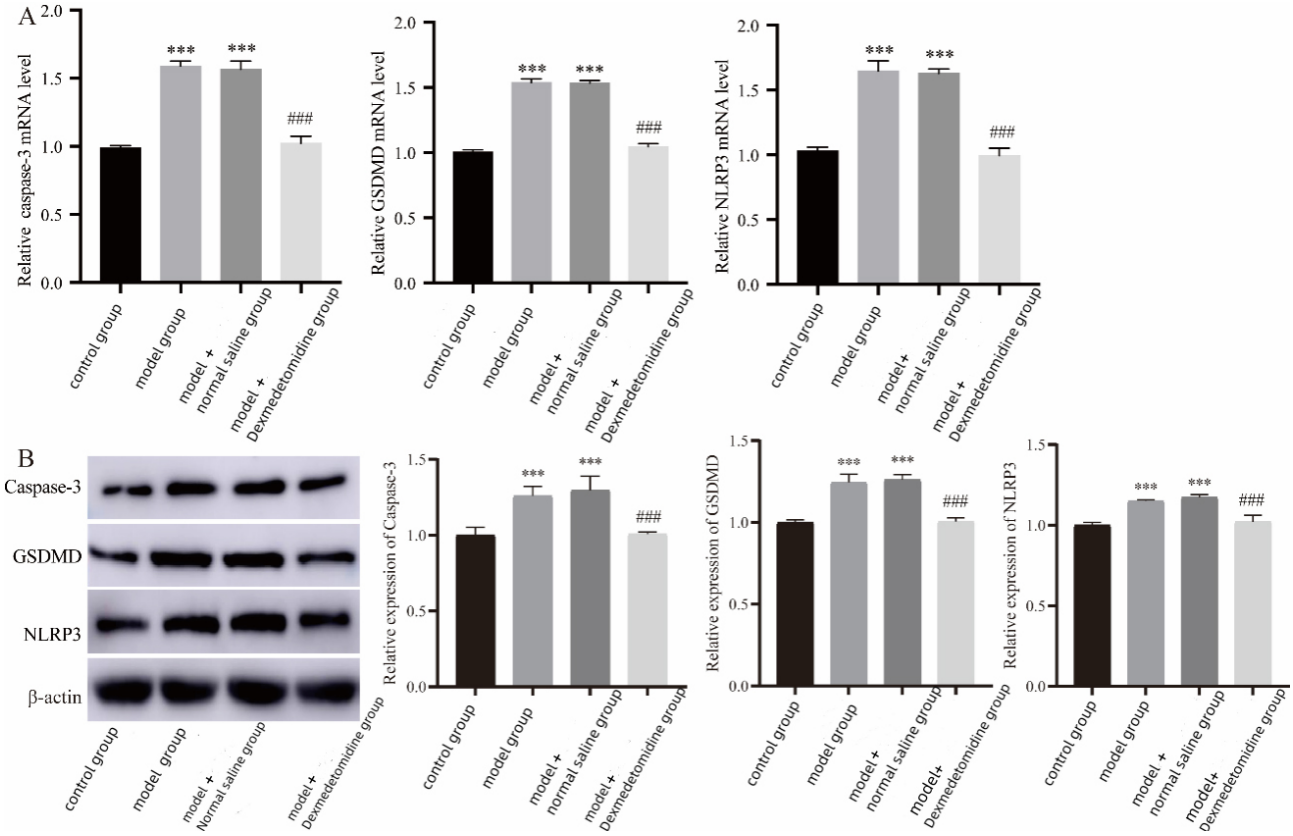

Fig. 4. Detection of pyroptosis-related protein expression before and after hip fracture in aged rats (n = 12). (A) mRNA levels of Caspase-3, GSDMD, and NLRP3 were measured by RT-qPCR. (B) Western blot was used to detect the protein expression levels of Caspase-3, GSDMD and NLRP3. Compared with control group, ***$p < 0.001$; Compared with the model group, ###$p < 0.001$.

Discussion

The purpose of this study is to investigate the effect of dexmedetomidine anesthesia in elderly patients undergoing hip fracture surgery. Orthopedic surgery is accompanied by severe postoperative pain, which may increase complications, including delirium, thereby affecting recovery, and dexmedetomidine is a good strategy to relieve postoperative pain [16]. Cognitive dysfunction is a very common event in patients with hip fracture [17]. This study analyzed the feasibility of dexmedetomidine in elderly patients undergoing hip fracture surgery.

A study on cognitive function in patients receiving dexmedetomidine has been published [18]. They showed that preoperative administration of dexmedetomidine was effective in protecting cerebral vessels, ameliorating cognitive dysfunction and impairment of attention network function, and improving postoperative quality of life. The results of this experiment showed that there was no significant change in cognitive ability after surgery compared with before surgery, and the scores of MMSE showed a trend of increase 24 h and 48 h after surgery. While these findings suggest that dexmedetomidine anesthesia may have an underlying protective effect on cognitive function in patients, it is important to note that this conclusion cannot be definitively drawn from the current experimental setting. A controlled comparison group, matched in terms of age, sex, weight, and having undergone hip fixation surgery but receiving a different anesthesia method, is necessary for a more accurate assessment of the effects of dexmedetomidine compared to alternative anesthesia methods. And there are also some earlier studies reporting that dexmedetomidine may reduce the occurrence of anesthesia-related cognitive dysfunction [19,20]. However, further studies are needed to determine the cognition-protective effects of dexmedetomidine in elderly patients undergoing hip fracture surgery and the underlying molecular mechanisms.

Elderly patients with hip fracture often experience agitation during surgery due to the trauma and discomfort caused by their position, especially those receiving intramedullary nailing. The sedative effect of dexmedetomidine may reduce the patient's agitation during surgery. In-

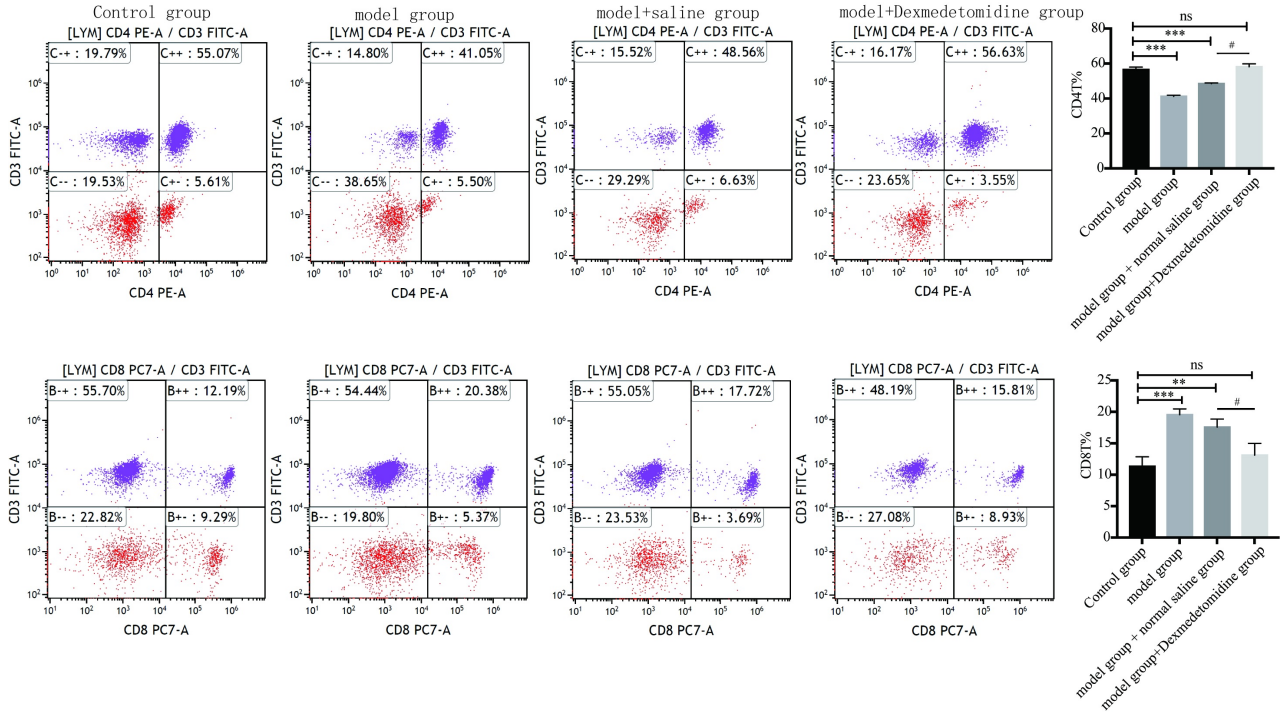

Fig. 5. CD4+T cell and CD8+T Cell levels measured by flow cytometry before and after hip fracture in the elderly (n = 12). $^{**}p < 0.01$, $^{***}p < 0.001$, $\#p < 0.05$. ns, no statistical difference.

creased IL-1β signaling has been implicated in many medical and psychiatric disorders, such as tissue damage, sepsis, as well as schizophrenia and mood disorders [21]. No significant changes in IL-1β expression after surgery were found in the results of this study. IL-18 levels decreased significantly in elderly patients after hip fracture surgery, suggesting that inflammation levels were reduced in elderly patients after hip fracture surgery. Therefore, the protective effect of dexmedetomidine on cerebral blood vessels may be manifested by a reduction in the levels of proinflammatory factors in cerebral blood vessels.

The present study also observed an increase in CD4+T cell levels in patients after surgery, suggesting that dexmedetomidine may have a positive effect on the immune function of patients. This is consistent with the results of study that have reported the effects of dexmedetomidine in reducing inflammation and improving immune function during hip replacement in the elderly [22]. In addition, pyroptosis aggravates myelin damage in various diseases and impairs cognitive function [23]. The levels of Caspase-3, GSDMD, and NLRP3 are significantly decreased, and these proteins are closely related to pyroptosis [24]. This result supports that dexmedetomidine is an α2 receptor agonist, and its neuroprotective effect may be related to the inhibition of inflammatory response and the reduction of pyroptosis [25,26].

The effect of dexmedetomidine on cognitive function was further explored in a rat hip fracture model. Behavioral tests showed that the exploratory movement of rats increased after surgery, suggesting that dexmedetomidine may improve the postoperative motor and cognitive function of rats [27]. Compared with pre-operation, the levels of Caspase-3, GSDMD and NLRP3 were significantly decreased and the level of CD4+T cells was increased in aged rats after hip fracture surgery. These results are almost consistent with those observed in our patients and further confirm the role of dexmedetomidine in attenuating pyroptosis and protecting immune function.

Conclusions

In conclusion, this study suggests that dexmedetomidine anesthesia may protect cognitive function, reduce pyroptosis, and improve immune function in elderly patients undergoing hip fracture surgery. These results provide a positive basis for the application of dexmedetomidine in hip fracture surgery in the elderly, which helps to optimize the surgical anesthesia program, reduce the risk of postoperative complications, and improve the postoperative recovery of patients. However, more studies are needed to validate these findings and explore the mechanism of action of dexmedetomidine.

Availability of Data and Materials

Data are available on request to the corresponding author for reasonable cause.

Author Contributions

XGQ designed the research study. XGQ, JBH and HC performed the research. XLC provided help and advice on the experiments. JBH analyzed the data. All authors contributed to the drafting or important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of the Fifth Affiliated Hospital of Xinjiang Medical University (XYDWFYLSH-2021-024) and followed the Helsinki Declaration. Patients were informed and signed the consent form before surgery. This study was also approved by the Animal Ethics Committee, with the ethical approval number: IACUC-20210530-67.

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Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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