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# Relations of heart-type and brain-type fatty acid-binding proteins with postoperative cognitive dysfunction in elderly patients undergoing spinal surgery

Minbo Jiang[1], Yang Li[1], Lei Cao[1], Jiwei Tian[2]*, Deguo Wang[1]*

## SUMMARY

**OBJECTIVE:** The aim of this study is to analyze the relations of heart-type fatty acid-binding protein (H-FABP) and brain-type fatty acid-binding protein (B-FABP) with postoperative cognitive dysfunction (POCD) in elderly patients undergoing spinal surgery.

**METHODS:** One hundred and twenty-five patients who underwent spinal surgery were enrolled in this study. According to whether patients had POCD within 5 days after surgery, the participants were divided into POCD group and non-POCD group. Before surgery and 6 h after surgery, the serum H-FABP and B-FABP contents were detected.

**RESULTS:** There were 33 (26.4%) patients in POCD group, and 92 (73.60%) patients in non-POCD group. After surgery, the serum H-FABP and B-FABP contents in POCD group were significantly higher than those before surgery, respectively ($p<0.05$), and those in non-POCD group were significantly lower than those before surgery, respectively ($p<0.05$). After surgery, the serum H-FABP and B-FABP contents in POCD group were significantly higher than those in non-POCD group, respectively ($p<0.05$).

**CONCLUSION:** The serum H-FABP and B-FABP contents are positively related to the occurrence of POCD in elderly patients undergoing spinal surgery.

KEYWORDS: H-FABP. B-FABP. Postoperative cognitive dysfunction. Elderly patients. Spinal surgery.

## INTRODUCTION

With the increase of elderly patients, the brain dysfunction that appears after general anesthesia is receiving more and more attention[1]. The neurocognitive changes related to surgery and anesthesia mainly include postoperative delirium and postoperative cognitive decline[2]. Although there is some overlap area, there are still differences in the occurrence time and clinical manifestations[3]. Complications of the central nervous system after surgery in the elderly patients are manifested as confusion, anxiety, personality changes, and memory impairment. These changes in personality, social ability, and cognitive ability and skills after surgery are called postoperative cognitive dysfunction (POCD)[4]. POCD is one of the common complications in elderly patients that may lead to delayed rehabilitation[5]. Early and accurate prediction of the occurrence of POCD is the key to prevention and control of POCD[6].

Fatty acid-binding protein (FABP) is a group of low-molecular weight proteins existing in cytoplasm. FABP is distributed in the tissues with active fatty acid metabolism and has the function of binding fatty acids and regulating cell metabolism. There are many types of FABP[7]. The study has found that the serum heart-type FABP (H-FABP) and brain-type

[1]Central Hospital of Songjiang District, Department of Orthopedics – Shanghai, China.
[2]People's Hospital of Jiangbei District, Department of Spinal Surgery – Chongqing, China.
*Corresponding authors: tianjws21@yeah.net; deguowang@yeah.net
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FABP (B-FABP) levels have high susceptibility for judging the brain injury[8]. Kok et al.[9] have studied the POCD in patients receiving heart surgery and they found that in patients with POCD, the serum B-FABP level 24 h after surgery is higher than that before surgery. Therefore, we hypothesized that the serum H-FABP and B-FABP were related with POCD in elderly patients undergoing spinal surgery. This study was designed to analyze the relations of serum H-FABP and B-FABP levels with POCD in elderly patients undergoing spinal surgery, in order to provide a scientific basis for the prediction of POCD in these patients.

# METHODS

## Patients

One hundred and twenty-five patients who underwent spinal surgery in our hospital from January 2019 to October 2019 were enrolled. There were 67 males and 58 females. There were 75 cases of lumbar spine surgery (among them, 25 cases with one-segment lumbar surgery, 32 cases with two-segment lumbar surgery, and 18 cases with three- or more segment lumbar surgery) and 50 cases of cervical spine surgery (24 cases with anterior cervical surgery and 26 cases with posterior cervical surgery). According to whether patients had POCD, the participants were divided into POCD group and non-POCD group. The demographic and clinical data of patients were shown in Table 1. There was no significant difference between two groups (p>0.05). This study was approved by the Medical Ethics Committee of People's Hospital of Jiangbei District, and informed consent was signed with patients or their families.

## Inclusion criteria and exclusion criteria

Inclusion criteria were as follows: the patients aged ≥60 years, the ASA grade was I–III, and the estimated operation time was ≥2 h. Exclusion criteria were as follows: the patients had severe respiratory or circulatory diseases; the patients had acute and chronic infections before surgery; the preoperative biochemical examination revealed renal dysfunction (i.e., blood creatinine >177 μmol/L) or active liver disease; the patients had history of myocardial infarction and cerebral infarction; the patients had a history of mental nervous system or taking related drugs; and the preoperative Mini-Mental State Examination (MMSE) score showed illiteracy level <17 points, primary school level <20 points, middle school level <22 points, and college and higher level <24 points.

## Anesthesia method

All patients were fasting for 8 h and drinking for 6 h before surgery. The patients were routinely monitored for aterial blood pressure (ABP), electrocardiogram (ECG), oxygen saturation ($SpO_2$), and bispectral index (BIS) after entering the room. Before the operation, a right internal jugular vein puncture was performed. The central venous catheter was routinely placed, and central venous pressure (CVP) was monitored. The anesthesia induction used 0.3 μg/kg sufentanil, 1.5–2.5 mg/kg propofol, and 0.6 mg/kg rocuronium bromide. A tracheal intubation anesthesia machine was used to control the breathing. The respiratory rate (RR) was 12 times/min, and the tidal volume (Vt) was 8–10 mL/kg. The anesthesia maintenance used target-controlled infusion of 2–4 μg/mL plasma concentration of propofol and intraoperative continuous pumping of rocuronium to maintain muscle relaxation. For intraoperative adjustment of

Table 1. Comparison of demographic and clinical data between postoperative cognitive dysfunction group and non-postoperative cognitive dysfunction group.

| Variables | POCD group | Non-POCD group | $t/\chi^2$ | p |
|---|---|---|---|---|
| n | 33 | 92 | | |
| Gender (n) | | | 0.081 | 0.782 |
| Male | 17 | 50 | | |
| Female | 16 | 42 | | |
| Age (years) | 69.53±5.41 | 67.14±6.49 | 1.892 | 0.061 |
| Body mass index (kg/m²) | 22.26±2.29 | 21.97±2.75 | 0.522 | 0.603 |
| Surgery type (n) | | | 0.007 | 0.934 |
| Lumbar spine surgery | 20 | 55 | | |
| Cervical spine surgery | 13 | 37 | | |
| Operation time (h) | 2.89±0.82 | 2.62±0.83 | 1.58 | 0.117 |
| Blood loss (mL) | 339.84±26.51 | 331.42±25.03 | 1.631 | 0.105 |

the dose of anesthetic drugs to maintain BIS at 40–60, intraoperative blood pressure fluctuations should not exceed 30% of the basic value. All patients were given patient-controlled intravenous analgesia (PCIA) after surgery. Of note, 2 μg/kg sufentanil+1 μg/kg dexmedetomidine+15 mg tropisetron were diluted to 100 mL with normal saline. The parameters were set to a background dose of 2 mL/h, an additional dose of 2 mL each time, and a lock time of 20 min. After the operation, the patient was sent to post-anesthesia care unit (PACU), and the tracheal tube was removed after awakening. After the hemodynamics was stable and the steward score was >4 points, the patient returned to the ward.

### Blood specimen collection and assessment of cognitive function

A 3 mL of central venous blood was collected before and after surgery. Cognitive function of patients was assessed with the MMSE scale on 1 day before surgery and 5 days after surgery. The total score was 30 points, and the normal value was 27–30 points. Those with a decrease of 2 points or more were considered to have cognitive decline and were diagnosed with POCD. The same number of patients with POCD as those with similar general conditions as sex, weight, ASA classification, blood loss, etc., were selected from patients who had never had POCD, and the serum H-FABP and B-FABP contents were determined together.

### Detection of H-FABP and B-FABP

The ELISA method was used to determine the serum contents of H-FABP and B-FABP before and 6 h after surgery. The specific method was performed according to the kit instructions.

### Statistical analysis

This study used SPSS 19.0 software for the statistical analysis. The enumeration data were presented as number and rate and were compared using $\chi^2$ test. The measurement data were presented as mean ± SD and were compared using *t*-test. $p<0.05$ was considered as statistically significant.

## RESULTS

### Occurrence of POCD

A total of 33 (26.40%) patients (POCD group) developed POCD at 5 days after surgery. Among them, 15 cases did not recover at 3 days, 10 cases did not recover at 5 days, 7 cases occurred newly 1–3 days after operation, and 1 case occurred 3–5 days after operation. Other 92 (73.60%) patients (non-POCD group) did not develop POCD.

### Comparison of serum H-FABP and B-FABP contents between POCD group and non-POCD group

Before surgery, the serum H-FABP and B-FABP contents in POCD group were significantly lower than those in non-POCD group, respectively ($p<0.05$). After surgery, each index in POCD group was significantly higher than that before surgery ($p<0.05$), and that in non-POCD group was significantly lower than that before surgery ($p<0.05$). In addition, after surgery, the serum H-FABP and B-FABP contents in POCD group were significantly higher than those in non-POCD group, respectively ($p<0.05$) (Figure 1).

Comparison of serum H-FABP and B-FABP contents between male and female patients

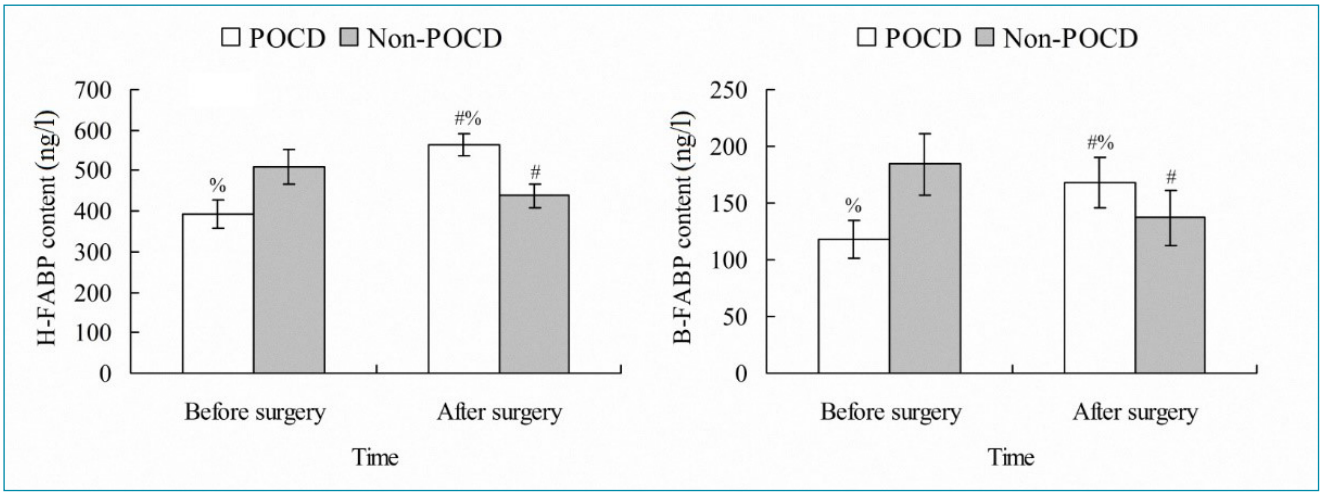


Figure 1. Comparison of serum heart-type fatty acid-binding protein and brain-type fatty acid-binding protein contents between postoperative cognitive dysfunction group and non- postoperative cognitive dysfunction group. #p<0.05 versus before surgery; %p<0.05 versus postoperative cognitive dysfunction D group.

Before and after surgery, there was no significant difference of serum H-FABP or B-FABP content between male and female patients, respectively ($p>0.05$). After surgery, the B-FABP content was significantly lower than before surgery for each gender ($p<0.05$) (Figure 2).

## DISCUSSION

The postoperative cognitive dysfunction is a common neurological complication in elderly patients[10]. In this study, the incidence of POCD within 5 days after surgery was similar to that reported by Moller et al.[11]. Changes in S100β protein and neuron-specific enolase (NSE) in serum can reflect brain damage and have been used to predict the occurrence of POCD[12]. Finding specific and sensitive predictive indicators of POCD is the key to prevent and control POCD. FABP is a group of low-molecular-weight proteins in the cytoplasm, which are involved in the regulation of fatty acid uptake and transport and enzyme activity. This study suggests that H-FABP and B-FABP are more sensitive and specific than S100 protein and NSE in the judgment of acute brain injury[8].

The results of this study show that compared with patients with non-POCD, the serum H-FABP content in patients with POCD increased significantly 6 h after surgery compared with that before surgery, and the results were similar to the earlier reports. Vupputuri et al.[13] found that H-FABP could hardly be detected in the peripheral circulation of normal people. When brain cells were damaged, it began to increase 1–3 h and reached a peak 6 h after operation. The content of B-FABP in serum was significantly increased 24 h after the study, and the incidence of POCD was significantly positively correlated with the changes of H-FABP and B-FABP contents. The results suggest that the increase of H-FABP and B-FABP in postoperative serum is closely related to the occurrence of POCD in patients. Kok et al.[9] confirmed that during the perioperative period of cardiac surgery neurocognitive dysfunction, the level of B-FABP in serum of patients with POCD 24 h after surgery was significantly higher than before surgery.

The pathogenesis of POCD is still unclear, involving disorders of the central nervous system, endocrine system, and immune system[14]. It is generally believed that POCD is based on the degeneration of the central nervous system in elderly patients, and it is caused by various factors such as acetylcholine, serotonin, norepinephrine, glutamic acid, and gamma-aminobutyric acid. Acute mental disorder syndrome is caused by further disorders of the neurotransmitter system. Cognitive dysfunction caused by elevated FABP may be related to its ability to regulate inflammatory cytokines through intracellular fatty acid-mediated signaling pathways. This study has shown that the downregulation of FABP can significantly reduce the synthesis of TNF-α and IL-6[15], and the overexpression of FABP can lead to increased synthesis of IL-7 and IL-18[16].

This study still has some limitations. First, the sample size of this study is relatively small, especially for the POCD group, which may affect the results. Second, the correlations of H-FABP, B-FABP, and other parameters have not been discussed. These issues should be solved in more in-depth research to make the outcomes more convincing.

## CONCLUSIONS

The serum H-FABP and B-FABP contents are positively related to the occurrence of POCD in elderly patients undergoing spinal surgery. This study has provided a certain scientific basis for the prediction of POCD in elderly patients undergoing spinal surgery.

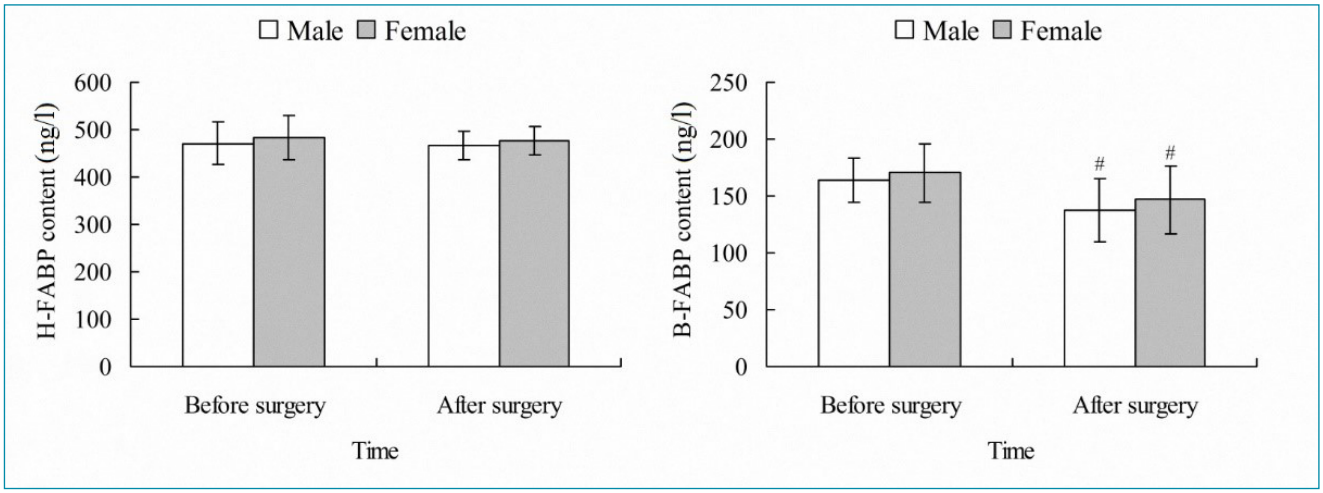


Figure 2. Comparison of serum heart-type fatty acid-binding protein and brain-type fatty acid-binding protein contents between male and female patients. #$p<0.05$ versus before surgery.

## AUTHORS' CONTRIBUTIONS

**MJ:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Visualization, Writing-original draft. **YL:** Conceptualization. **LC:** Data curation, Software. **JT:** Project administration, Supervision, Validation, Writing—review and editing. **DW:** Project administration, Supervision, Validation, Writing—review and editing. All authors have read and agreed to the published version of the manuscript.

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