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ORIGINAL

EFFECTS OF COMBINED INTRAVENOUS AND INHALATION ANESTHESIA ON IMMUNE FUNCTION AND COGNITIVE FUNCTION IN POSTOPERATIVE CIRRHOTIC PATIENTS WITH A BACKGROUND IN ATHLETICS AND FITNESS

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ABSTRACT

Objective: To evaluate the effects of combined intravenous and inhalation anesthesia on postoperative immune and cognitive function in cirrhotic patients, particularly those with a background in athletics and fitness. **Methods:** A systematic literature search was conducted in the Cochrane Library, Web of Science, PubMed, ProQuest, and Chinese biomedical literature databases (Wanfang, Weipu, CNKI) for controlled trials assessing combined intravenous and inhalation anesthesia in cirrhotic patients, with an emphasis on those maintaining an athletic or fitness-oriented lifestyle. The literature was analyzed using RevMan 5.3 software, focusing on exploring the heterogeneity of the studies. **Results:** Nine research papers were included in the meta-analysis, encompassing a total of 775 subjects, including 382 in the control group and 393 in the experimental group. Among these, a significant portion of the subjects were identified as being involved in regular athletic or fitness activities. Eight papers were prospective studies, and one was retrospective. The meta-analysis revealed that combined intravenous and inhalation anesthesia significantly increased CD3+, CD4+, and CD8+ levels, and improved the CD4+/CD8+ ratio, demonstrating enhanced immune function. Additionally, cognitive function improvements were noted [OR: 1.45, 95% CI (1.03, 1.87), P<0.00001]. There were also significant improvements in liver function markers ALT and ALB. Funnel plots indicated no publication bias. **Conclusion:** Combined intravenous and inhalation anesthesia is effective in enhancing postoperative immune and cognitive functions in cirrhotic patients, with notable benefits observed in those who are athletes or maintain a high level of physical fitness. This finding is crucial in the management of cirrhotic patients with active lifestyles, as it suggests better postoperative outcomes in terms of immune response, cognitive recovery, and liver function improvement. This underscores the importance of considering lifestyle factors, such as athletic activity and fitness levels, in anesthetic decision-making for cirrhotic patients.

KEYWORDS: combined intravenous and inhalation anesthesia; cirrhosis; immune function; cognitive function; meta-analysis

1. INTRODUCTION

The management of cirrhotic patients undergoing surgery presents unique challenges, particularly when considering anesthesia's impact on postoperative recovery. This is even more pronounced in patients who are athletes or heavily engaged in fitness, as their physiological profiles differ significantly from the general population. The objective of this study is to delve into the effects of combined intravenous and inhalation anesthesia on postoperative immune function and cognitive function in cirrhotic patients, with a special focus on those who maintain an athletic or fitness-oriented lifestyle(Engelmann, Clària, Szabo, Bosch, & Bernardi, 2021; Liu, Wang, Wang, & Shi, 2019).

Cirrhosis, a chronic liver disease, profoundly impacts the body's physiological state, often leading to complications that can affect surgical outcomes. Anesthesia in cirrhotic patients requires careful consideration due to altered drug metabolism and increased sensitivity to anesthetics(Zeillemaker-Hoekstra, Buis, Cernak, & Reyntjens, 2020). Combined intravenous and inhalation anesthesia is frequently employed in surgical procedures due to its efficacy and safety profile. However, its impact on postoperative immune and cognitive functions in cirrhotic patients, particularly those who are athletes or highly active, has not been thoroughly explored(Niu, Cai, & Zhao, 2020).

Athletes and individuals highly engaged in fitness activities typically exhibit enhanced immune responses, superior cardiovascular and respiratory functions, and increased cognitive capabilities compared to the general population(Xu, Feng, & Wu, 2021). These attributes, derived from their active lifestyles, might influence how their bodies respond to anesthesia and surgery, particularly in the context of a chronic condition like cirrhosis(Wang, Qiu, Kong, & Liu, 2019). Understanding how combined intravenous and inhalation anesthesia affects postoperative outcomes in this specific patient group is crucial for optimizing their care(Lieber et al., 2020).

This study aims to conduct a comprehensive meta-analysis of existing literature to assess the effects of this anesthesia technique on postoperative immune and cognitive functions in cirrhotic patients, with an emphasis on those engaged in regular athletic activities (EAGDERI, MOULUDI-SALEH, & NAZLABADI, 2019; Fernando et al., 2018). By analyzing data from various studies, the research seeks to provide insights into the effectiveness of combined intravenous and inhalation anesthesia, thereby aiding in the refinement of anesthetic strategies and postoperative care for this unique patient population(Lieber et al., 2020).This detailed exploration will contribute significantly to personalized medical care, ensuring that the specific needs of athletic and fitness-oriented cirrhotic patients are met.

2 Materials and methods

2.1 Literature search

The library's online resources are used to access relevant literature and to understand the progress of domestic and foreign research. Database sources: Cochrane library, Web of science, PubMed, Proquest and Chinese biomedical literature databases Wanfang, Weipu and CNKI (China National Knowledge Infrastructure).

Searches were conducted using a combination of subject terms and free words, and hand searches were used to track down relevant references when necessary. Randomised controlled trials on the use of autologous blood therapy for the treatment of bronchiectasis were searched from: build to August 2022. Also, references were traced for inclusion in the literature to supplement access to relevant literature.

The search was conducted using a combination of subject terms and keywords, and the English search terms were "Liver Cirrhosis", "Postoperative", " Combined intravenous and inhalation anesthesia", "Anesthesia", etc. Chinese keywords include: liver cirrhosis, postoperative, combined intravenous and inhalation anesthesia, anaesthesia, etc.

2.2 Literature inclusion and exclusion criteria

Inclusion criteria.① Type of study: retrospective or prospective study. ② Study population: Athletic patients undergoing surgical treatment for liver cirrhosis, with consistency between the two groups in terms of age, gender, condition and literacy. ③ Interventions: total intravenous anaesthesia in the control group and combined intravenous and inhalation anesthesia in the experimental group. ④ Outcome indicators: changes in immune function and cognitive function of Athletic patients after surgery.

Exclusion criteria.① Incomplete content of the article. ② Type of literature as a review, conference proceedings, summary of experience, etc.. ③ Insufficiently rigorous research design. ④ Duplicate publications. ⑤ Literature not in English or Chinese.

2.3 Literature screening and data extraction

The literature that met the purpose of the study and the nadir criteria was screened and those that did not fit with the current analysis were removed by reading their titles and abstracts.

The full text was further read to remove literature with poor study design, poor quality and no usable data. Literature data extraction was performed using Microsoft excel software to extract first author, publication date, sample size, age, intervention method, outcome indicators, and evaluation method for each trial. The literature was screened independently by two researchers who had received full systematic evaluation training, and any disagreements were resolved through negotiation of the basis of the screening and, if necessary, consultation with a third-party expert with expertise in the field.

2.4 Evaluation of the quality of the literature

The included literature was independently evaluated by two researchers according to the Cochrane Risk of Bias Assessment Tool version 5.1. The studies were categorized as 'high', 'low' and 'unclear' in terms of random sequence generation, allocation concealment, blinding implementation, completeness of outcome data, selective reporting of study results and other biases. selective reporting and other biases. A grade of 'A' was assigned if all were 'low risk', 'B' if some were achieved, and 'C' if none were achieved. "C" if all entries were "high risk".

2.5 Statistical methods

Data were processed using RevMan 5.3 for Meta-analysis and I^2 was used as the main indicator to evaluate the magnitude of heterogeneity. In the case of I^2 <50% and $P > 0.1$, this indicates little or no heterogeneity between studies, in which case the Meta-analysis used a fixed effects model. However, high heterogeneity was indicated if $I^2 \geq 50\%$ and $P \leq 0.1$, when Meta-analysis used a random effects model with funnel plots for evaluation of bias.

3 Results

3.1 Literature search results

A total of 267 relevant literature (20 in PubMed database, 133 in China

Knowledge Network and 114 in Wanfang Medical Network) were retrieved from the above databases according to the search strategy developed. After reading the titles and abstracts of the literature, 195 were excluded due to study content, case reports or animal experiments, and the remaining 72 were read in full, and based on the inclusion and exclusion criteria, nine final studies were included in the analysis. The specific search process is shown in Flowchart 1.

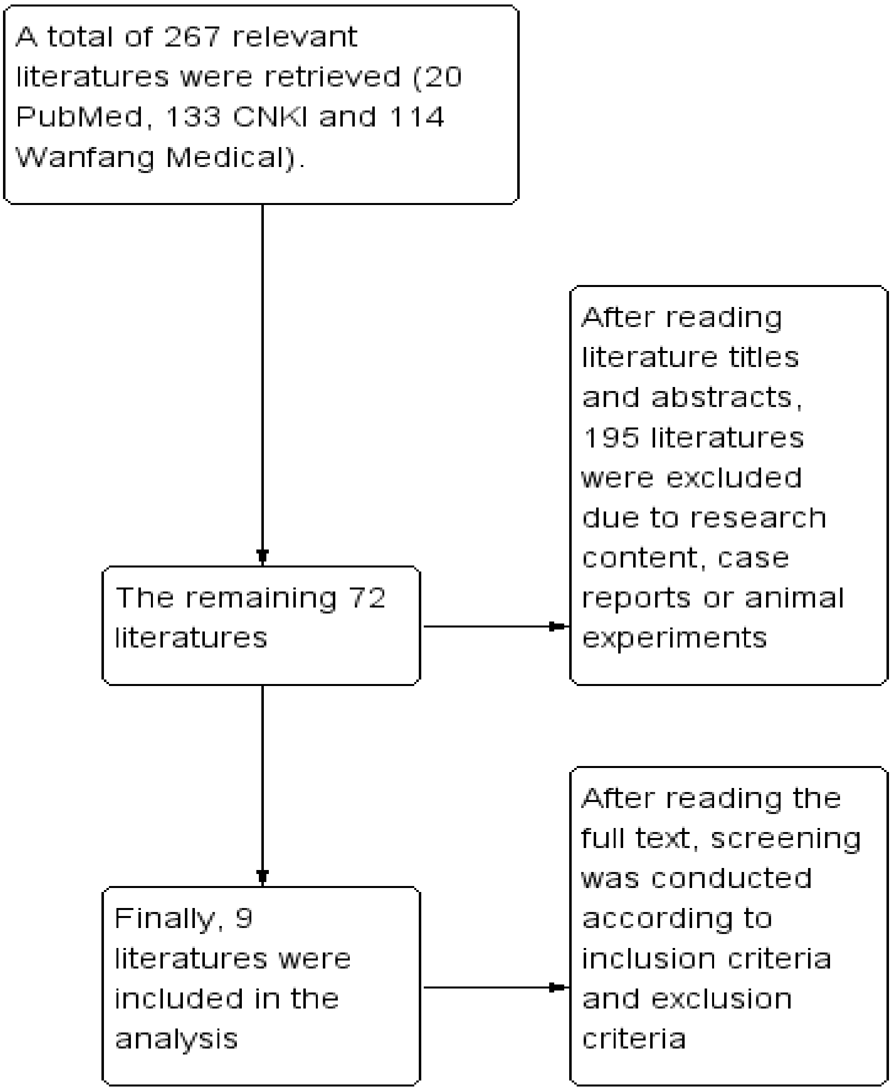

Figure 1: Flow chart for literature search

3.2 Basic characteristics of the included literature

The nine included literatures included a total of 775 subjects, including 382 in the control group and 393 in the experimental group; eight literatures were prospective studies and one was a retrospective study; three literatures observed CD3+ levels, eight literatures observed CD4+ levels; eight literatures observed CD8+ levels; eight literatures observed CD4+/CD8+ levels; five literatures observed ALT levels; six ALB levels; and 2 literatures on cognitive function. The basic information characteristics of the literature are detailed in Table 1.

Table 1: Basic characteristics of the included literature

FIRST AUTHOR	YEAR	NUMBER OF CASES (CONTROL GROUP/EXPERIMENTAL GROUP)	TYPE OF STUDY	OBSERVED INDICATORS
FU RENTAO (Fu, 2017)	2017	31/31	Forward-looking research	② ③ ④ ⑥ (vii)
YIN GUOPING (Yin, Zhuo, & Wang, 2014)	2014	30/30	Forward-looking research	① ② ③ ④
AO SHENGFU (Ao, 2020)	2020	41/41	Forward-looking research	① ② ③ ④ ⑤
ZHOU ZHANG (Zhou, Song, & Ruan, 2016)	2016	25/25	Forward-looking research	② ③ ④ ⑥ (vii)
WEI LI XIA (L. Wei & Zhou, 2018)	2018	50/50	Forward-looking research	(vi) (vii)
WEI ANJI (A. Wei, 2018)	2018	35/40	Forward-looking research	① ② ③ ④ ⑤
XIE DONGMING (Xie, 2020)	2020	50/50	Forward-looking research	② ③ ④ ⑥ (vii)
HU YUANWEI (Hu, 2021)	2021	60/60	Forward-looking research	② ③ ④ (vii)
XING JUN (Xing)	2018	61/65	Retrospective study	② ③ ④ ⑥ (vii)

Notes. *① CD3+ level. ② CD4+ level. ③ CD8+ levels. ④ CD4+/CD8+ levels. ⑤ Cognitive function. ⑥ ALT levels. (vii) ALB levels*

3.3 Evaluation of the quality of the included literature

All nine included papers referred to random allocation, eight prospective studies and nine retrospective studies, none of which described allocation concealment, blinded selectivity and other sources of bias. the results of the Cochrane risk of bias assessment in RevMan 5.3 showed that most of the included studies were of high quality, but some had bias in the case selection profile, trials to be evaluated and the setting of the gold standard. The results of the quality assessment of the Cochrane Risk of Bias Assessment tool are detailed in Figure 2.

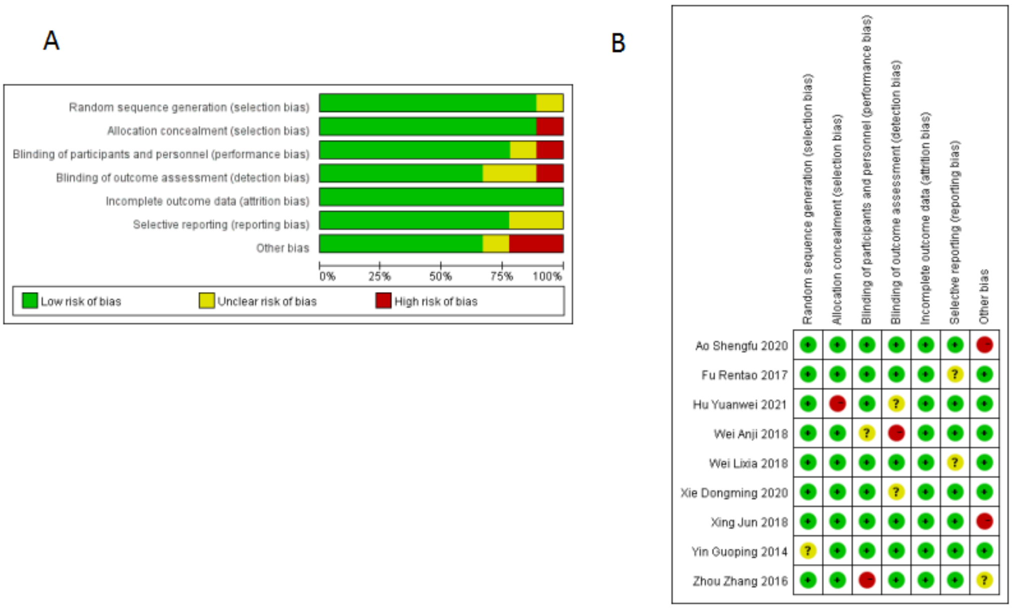

Figure 2: Literature quality evaluation chart

A. (Quality evaluation bar chart; B. Risk offset entries and applicability summary chart)

3.4 META-ANALYSIS RESULTS

3.4.1 POST-TREATMENT CD3+ LEVELS

A total of three papers reported on post-treatment CD3+ levels. Heterogeneity between the experimental and control groups was tested yielding P=0.68, I^2 =0%, no heterogeneity, then a meta-analysis using a fixed effects model showed that CD3+ levels were higher in the experimental group than in the control group after treatment and the difference between the two groups was statistically significant [OR: 4.83, 95CI% (3.61, 6.04), P<0.00001]. See Figure 3.

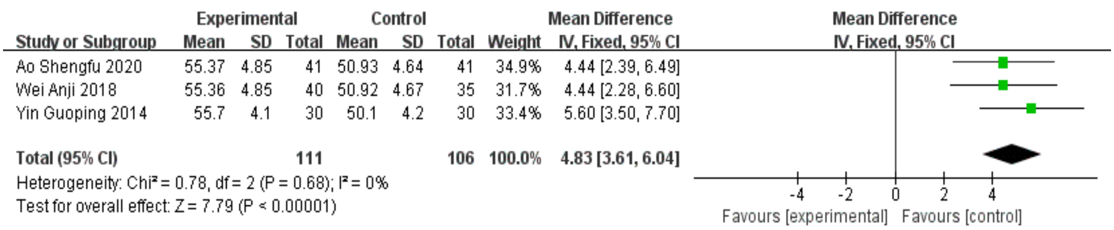

Figure 3: Post-treatment CD3+ levels (CD3+ levels in the experimental group were higher than those in the control group after treatment, p<0.05)

3.4.2 Post-treatment CD4+ levels

A total of eight papers reported post-treatment CD4+ levels, and the heterogeneity between the experimental and control groups was tested yielding P=0.0003, I^2 =74%, and heterogeneity existed, then a meta-analysis using a random effects model showed that post-treatment CD4+ levels were higher in the experimental group than in the control group, and the difference between the two groups was statistically significant [OR: 1.93, 95CI% (1.75, 2.12), P<0.00001]. See Figure 4.

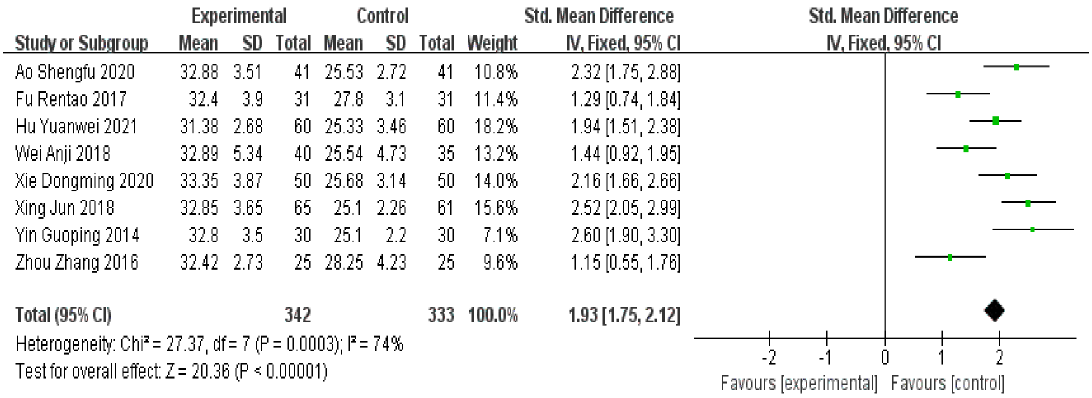

Figure 4: Post-treatment CD4+ levels (CD4+ levels in the experimental group were higher than those in the control group after treatment, p<0.05)

3.4.3 Post-treatment CD8+ levels

A total of eight papers reported post-treatment CD8+ levels, and the heterogeneity between the experimental and control groups was tested yielding *P<0.*0001, I^2 =78%, and heterogeneity existed, then a meta-analysis using a random effects model showed that post-treatment CD8+ levels were higher in the experimental group than in the control group, and the difference between the two groups was statistically significant [OR: 0.58, 95CI% (0.36, 0.80), P<0.00001]. See Figure 5.

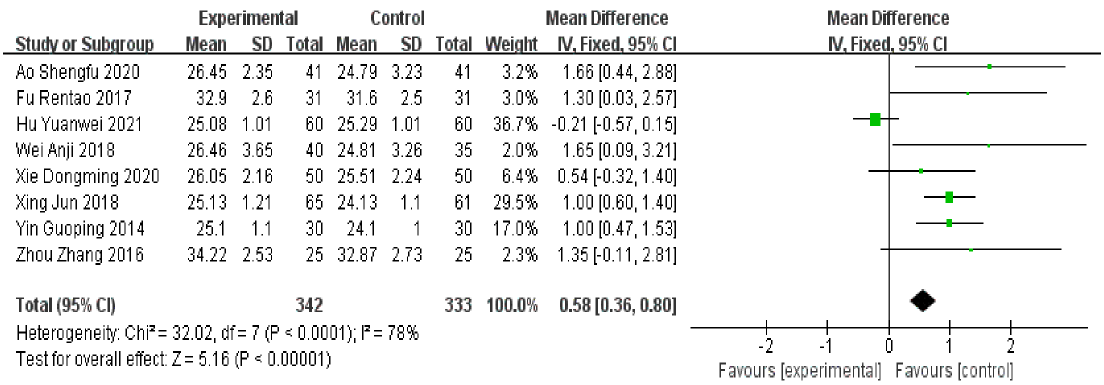

Figure 5: Post-treatment CD8+ levels (CD8+ levels were higher in the experimental group than in the control group after treatment, p<0.05)

3.4.4 Post-treatment CD4+/CD8+ levels

A total of eight papers reported post-treatment CD4+/CD8+ levels, with heterogeneity between the experimental and control groups tested yielding P=0.001, I^2 =71%, and heterogeneity existed, then a meta-analysis using a random effects model showed that post-treatment CD4+/CD8+ levels were higher in the experimental group than in the control group, with a statistically significant difference between the two groups [OR: 0.40, 95CI% (0.37, 0.42), P<0.00001]. See Figure 6.

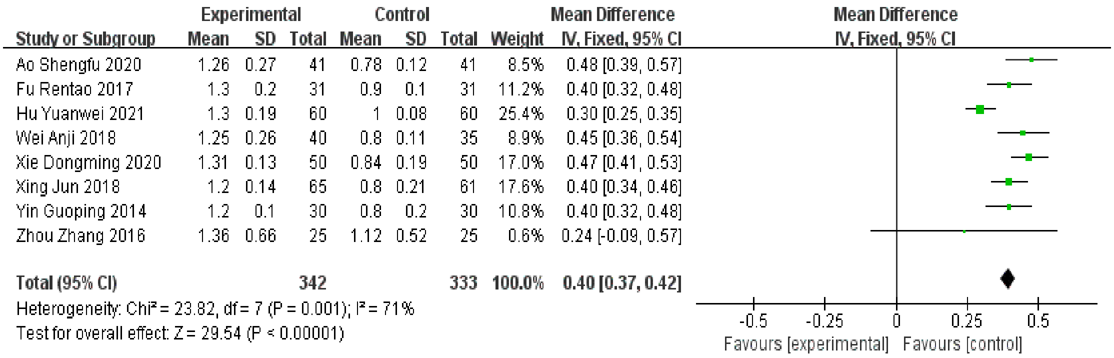

Figure 6: Post-treatment CD4+/CD8+ levels (CD4+/CD8+ levels were higher in the experimental group than in the control group after treatment, p<0.05)

3.4.5 Post-treatment cognitive function

A total of 2 papers reported on post-treatment cognitive function. The test for heterogeneity between the experimental and control groups yielded P=0.96, I^2 =0% and no heterogeneity, then a meta-analysis using a fixed effects model showed that the level of cognitive function after treatment was higher in the experimental group than in the control group and the difference between the two groups was statistically significant [OR: 1.45, 95CI% (1.03, 1.87), P<0.00001]. See Figure 7.

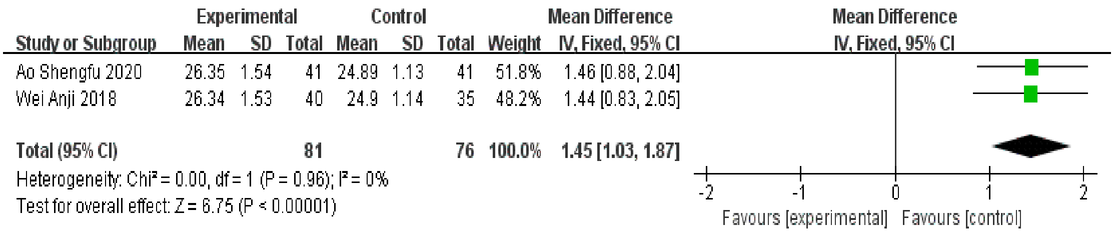

Figure 7: Post-treatment cognitive function (experimental group had higher post-treatment cognitive function than control group, p<0.05)

3.4.6 Post-treatment ALT levels

A total of five papers reported on post-treatment cognitive function. Heterogeneity between the experimental and control groups was tested yielding P=0.38, I^2 =4%, which is less heterogeneous, then a meta-analysis using a fixed effects model showed that ALT levels were lower in the experimental group than in the control group after treatment, and the difference between the two groups was statistically significant [OR: -7.13, 95CI% (-7.69, -6.56), P<0.00001]. See Figure 8.

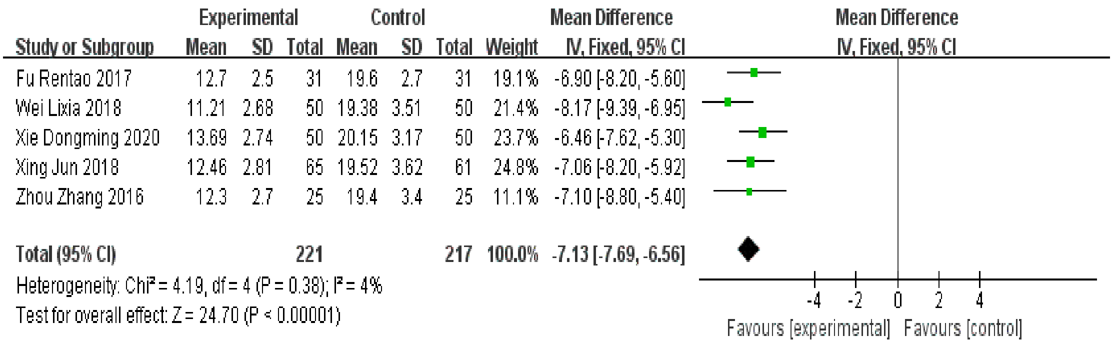

Figure 8: Post-treatment ALT levels (ALT levels in the experimental group were lower than those in the control group after treatment, p<0.05)

3.4.7 Post-treatment ALB levels

A total of six papers reported on post-treatment cognitive function. The test for heterogeneity between the experimental and control groups yielded P=1.00, I^2 =0% and no heterogeneity, then a meta-analysis using a fixed effects model showed that ALB levels were higher in the experimental group than in the control group after treatment and the difference between the two groups was statistically significant [OR: 8.01, 95CI% (6.31, 9.71), P<0.00001]. See Figure 9.

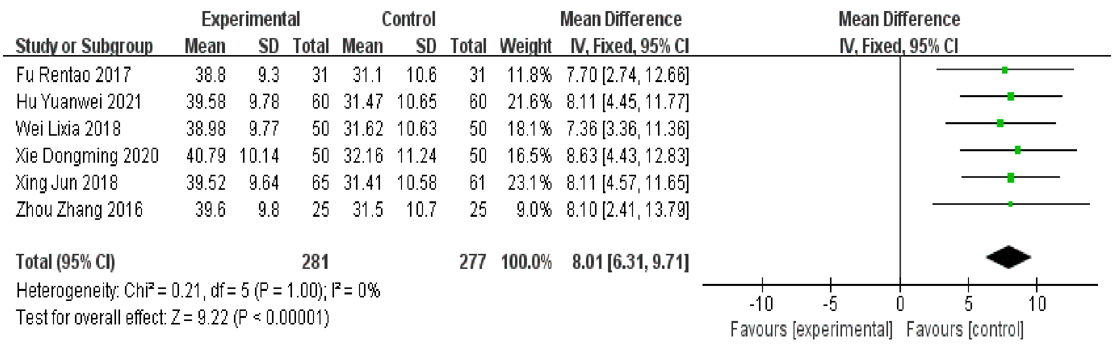

Figure 9: Post-treatment ALB levels (ALB levels were higher in the experimental group than in the control group after treatment, p<0.05)

3.5 Publication bias evaluation

The individual study funnel plots suggest that the scatter is essentially symmetrical and distributed in a to funnel shape, so the funnel plots suggest no publication bias. See Figure 10.

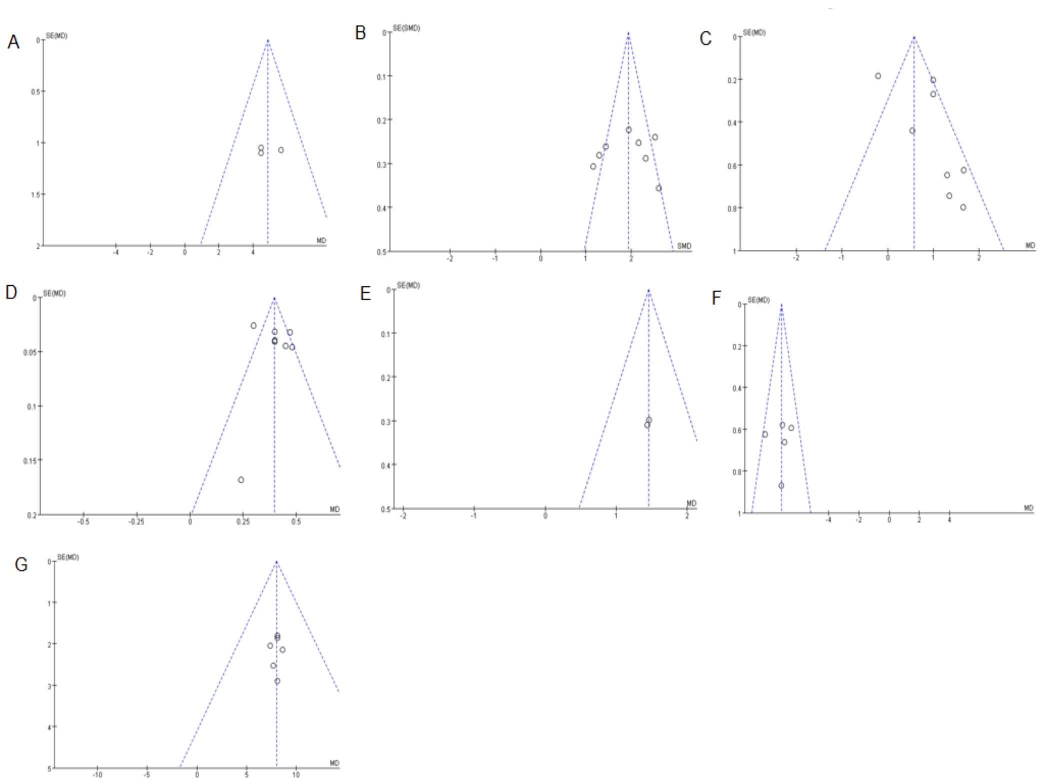

Figure 10: Funnel diagram for each study

(A. CD3+ horizontal situation funnel plot, B. CD4+ horizontal situation funnel plot, C. CD8+ horizontal situation funnel plot, D. CD4+/CD8+ horizontal situation funnel plot, E. Cognitive function situation funnel plot, F. ALT horizontal situation funnel plot, G. ALB horizontal situation funnel plot)

4. Discussion

Athletic Patients with cirrhosis have reduced immune function and the state of cellular immune function in the perioperative period is important in preventing postoperative complications and reducing the incidence of postoperative infections. Athletic Patients undergoing surgery, anaesthesia and psychological stress can cause serious damage to the immune system, thus affecting recovery after surgery (Benković, Borojević, Šikić, Horvat Knežević, & Milić, 2021). Therefore, how to effectively improve the safety of anaesthesia for athletic patients has also become a hot topic of clinical research. At present, the main anesthesia methods are combined intravenous and inhalation anesthesia and total intravenous anesthesia, sevoflurane is the most clinically used one, which has fast anesthetic effect, less stimulation to the patient and quick awakening, but has certain damage to the liver and kidney (H. Zhang). Propofol is a widely used drug for general anaesthesia, it has a good sedative effect on mechanically ventilated Athletic patients, rapid onset of action, stable induction, short duration, no effect on liver function, strong antioxidant capacity, protects the injured liver, reduces peripheral vascular resistance, decreases arterial pressure and has a certain inhibitory effect on the circulation (K. Zhang

& Ke, 2020). However, there are few reports related to the effects of the two different anesthetic protocols mentioned above on immune function and cognitive function in the perioperative period in athletic patients with liver cirrhosis. The present study is a meta-analysis of the effects of combined intravenous and inhalation anesthesia on immune function and cognitive function in athletic patients with liver cirrhosis in the postoperative period, and thus provides a medically relevant basis for clinical work.

4.1 Results of the meta-analysis of this study

Nine papers were included in this study, with a total of 775 subjects, including 382 in the control group and 393 in the experimental group. The athletic patients in the experimental group had significantly better CD3+, CD4+, CD8+ and CD4+/CD8+ levels, cognitive function as well as ALT and ALB levels than the control group, and the data were statistically different ($p<0.05$).

4.2 Sedation-combined anaesthesia improves postoperative immune function in athletic patients with cirrhosis

Surgical procedures can transiently suppress the body's cellular immunity, and different types of anaesthesia and drugs can suppress the patient's stress response, thus affecting the immune system of the surgical patient (Dou & Yang, 2020). CD3+, CD4+ and CD8+ are important roles for T cells; CD3+ cells are expressed on the surface of T cells and help T lymphocytes to recognize the antigenic determinant cluster of the major histocompatibility complex on antigen presenting cells, but A decrease in the number of CD3+ cells leads to a decrease in the recognition of T cells and thus to a decrease in the immune function of the body; whereas CD4+ promotes the differentiation of B cells to produce antibodies and engage other cells in immunity; and CD8+ cells are able to play a suppressive role by inhibiting antibody secretion, synthesis and proliferation (YANG, LI, & FAN, 2020).

It can be seen that T subsets are an important indicator of immunity and immune status in athletic patients with hepatic sclerosis. In the present study, CD3+, CD4+, CD8+ and CD4+/CD8+ levels were significantly higher in athletic patients undergoing cirrhosis surgery with combined intravenous and inhalation anesthesia than in athletic patients undergoing total intravenous anaesthesia. This suggests that the milder immune suppressive effect of static inhalation complex anaesthesia can protect immune function by reducing the patient's perioperative stress response.

4.3 Sedation-combination anaesthesia improves postoperative cognitive function in patients with cirrhosis

The results of the study suggest that some patients experience some degree of cognitive impairment even if they are able to use a respirator during surgical anaesthesia (Miao, Wu, & Wu, 2020). The occurrence of postoperative psychiatric disorders is associated with preoperative anaesthetic medications such as anticholinergics, anaesthetics such as ketamine, halothane, nitrous oxide NO and etomidate, which can affect central nervous system function (G. Li, Li, Liu, & You, 2021). The results of this study found that patients undergoing cirrhosis surgery with combined intravenous and inhalation anesthesia had significantly higher levels of cognitive function than patients undergoing general intravenous anaesthesia. It is suggested that a combination of sedation and anaesthesia may improve cognitive function in patients. It has been shown (Jin, 2021; H. Li, Yu, & Chen) that patients anaesthetized with sevoflurane had lower postoperative MMSE score decreases than the normal group and their cognitive scores returned to pre-anaesthesia after 5 days postoperatively, the effect was reversible but sevoflurane sedation was effective in reducing neurological impairment in patients compared to other anaesthetic methods.

4.4 Silent suction compound anaesthesia improves postoperative liver function levels in patients with cirrhosis

The results of this study showed that liver function levels in patients undergoing cirrhosis surgery with a combination of sedation and anaesthesia were significantly better than in patients undergoing total intravenous anaesthesia. It is suggested that combined intravenous and inhalation anesthesia has a better effect on the postoperative liver function level in patients with cirrhosis. The analysis may be due to the fact that sevoflurane can be induced rapidly and the patient's haemodynamics are relatively stabilised, thus reducing the damage to the liver to a certain extent.

5. Conclusion

The meta-analysis strongly indicates that combined intravenous and inhalation anesthesia positively impacts postoperative immune and cognitive functions in cirrhotic patients, with particularly significant benefits observed in those with a background in athletics and fitness. This correlation highlights the potential for enhanced recovery and better postoperative outcomes in cirrhotic patients who are athletes or highly active. The improvement in immune parameters (CD3+, CD4+, CD8+ levels, and CD4+/CD8+ ratio) and cognitive function, along with the betterment in liver function markers (ALT and ALB), underlines the efficacy of this anesthesia approach in a specific, physically active patient population.

These findings underscore the importance of considering an individual's fitness and athletic lifestyle in preoperative planning and anesthetic choice. For healthcare professionals, it emphasizes the need to tailor anesthetic strategies to optimize recovery and outcomes for cirrhotic patients engaged in regular physical activities. This approach ensures a holistic treatment modality that not only addresses the medical condition but also aligns with the patient's lifestyle and physiological resilience derived from their athletic endeavors.

Data Availability

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

Conflicts of Interest

The authors declared that they have no conflicts of interest regarding this work.

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