## **Medical Research**

ISSN	2664-0333 (print)
ISSN	2664-0341 (online)
DOI	10.6913/mrhk
Founded	July 2019
Publishing cycle	A Quarterly
Published by	Creative Publishing Co., Limited
Address	Flat A, 14/F, Kam Bit Building, 16 Victory Avenue, Ho Man Tin, Kowloon City District, Kowloon, Hong Kong, PR CHINA
Telephone	+852-95688358 +86-18565685800
Website	https://mrhk.cc
E-mail	wtocom@gmail.com

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## **Medical Research**

ISSN 2664-0333(Print) 2664-0341(online) Volume 6 Issue 3 Date of publication 30 September 2024 DOI 10.6913/mrhk Founded in July 2019 A quarterly

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## Research on the Application of Mind Map in Emergency Triage of Acute Abdomen

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## Abstract

**Objective:** To explore the application effect of Mind Map in the emergency triage of Acute Abdomen. **Methods:** Thirty-six patients with Acute Abdomen admitted to the emergency department of our hospital from July 2021 to December 2021 were set as the control group, during which the conventional emergency triage process was implemented. Another 36 patients with Acute Abdomen admitted to the emergency department of our hospital from January 2022 to June 2022 were set as the experimental group, during which the Mind Map tool was used for triage. The accuracy of triage and the time taken for triage assessment were compared between the two groups. **Results:** The accuracy of pre-triage classification and grading in the experimental group was significantly higher than that in the control group, and the time taken for triage assessment was significantly shorter than that in the control group. **Conclusion:** The pre-triage process based on Mind Map can significantly improve the accuracy and efficiency of emergency triage for Acute Abdomen, achieving standardized management of Acute Abdomen triage, and is worth promoting.

Keywords Acute Abdomen; Mind Map; Emergency Triage

Acute Abdomen is a critical condition characterized by sudden onset abdominal pain, with features such as rapid onset, complex condition, and swift progression. Delayed diagnosis and treatment can cause severe harm, even death<sup>[1]</sup>. Therefore, rapid and accurate triage and early treatment are crucial. The Mind Map, an emerging teaching tool in recent years, organizes and summarizes dull content by combining text and images, presenting hierarchical relationships of various themes to facilitate memory and learning for learners<sup>[2]</sup>. This study introduces the Mind Map tool to assist emergency department nursing staff in quickly and accurately triaging Acute Abdomen, thereby making the triage process more standardized and regulated. The specific report is as follows.

## 1 Data and Methods

## 1.1 Clinical Data

From July 2021 to December 2021, 36 patients with Acute Abdomen admitted to our hospital's emergency department were designated as the control group, including 18 males and 18 females, aged 23 to 75 years, with an average age of (42.83±14.25) years. Another 36 patients with Acute Abdomen admitted to our hospital's emergency department from January 2022 to June 2022 were designated as the experimental group, including 17 males and 19 females, aged 21 to 77 years, with an average age of (46.94±17.15) years. There was no significant difference in general data between the two groups (P > 0.05). All patients in both groups were older than 14 years and could clearly answer questions related to disease diagnosis and treatment asked by medical staff. Patients whose causes of Acute Abdomen could not be diagnosed or whose case data were incomplete were excluded.

## 1.2 Methods

The control group implemented the routine emergency triage process, specifically: the emergency nurse, according to the SOAP formula, inquired about the patient's chief complaint, conducted vital signs and related physical examinations, recorded the patient's chief complaint and accompanying symptoms (S), signs and abnormal findings (O), made a preliminary diagnosis (A), and performed injury classification (P), and then triaged the patient.

The experimental group used the Mind Map tool for pre-triage, with specific content as follows:

(1) Establishment of the Mind Map working group: The Mind Map group consists of one emergency department physician, the head nurse, and two nurses. The group members are mainly responsible for creating the Mind Map and providing relevant triage training to the emergency department nursing staff.

(2) Mind Map creation: The Mind Map group reviewed literature and analyzed the current issues in the triage of Acute Abdomen in the hospital's emergency department. They identified "Acute Abdomen Pre-Triage" as the core keyword, branching out into eight primary branches: observation, inquiry, examination, measurement, grading, and departmental classification, each representing the relevant work content of the emergency triage nurses, as shown in Figure 1.

(3) Mind Map training: The Mind Map group first conducted theoretical teaching for the department's nursing staff, explaining the key points and essentials of Acute Abdomen condition

assessment, triage strategies for patients with unclear symptoms or causes, and introduced the content and precautions of each branch of the created Mind Map. Then, they used scenario simulation methods for practical teaching to further consolidate the nurses' proficiency in applying the Mind Map.

(4) Clinical application of the Mind Map: After training, the created Mind Map was printed and laminated, distributed to each nurse (and also shared in the department's WeChat work group), and pasted on the triage desk for easy reference and study by the nurses.

1			
Group	Number of	Accuracy Rate of Pre-Triage	Accuracy Rate of
	Cases	Departmental Classification	Grading
Experimental	36	36 (100.00)	35 (97.22)
Group	50	50 (100.00)	55 ()1.22)
Control Group	36	30 (83.33)	28 (77.78)
P Value		0.025	0.033

Table 1 Comparison of the Accuracy Rates of Pre-Triage Departmental Classification and Grading Between Two Groups [n (%)]

## 1.3 Observation Indicators

Record and compare the pre-triage accuracy rate, grading accuracy rate, and the time required for triage assessment between the two groups. Among them, pre-triage accuracy refers to the triage nurse's ability to accurately direct acute abdomen patients to the appropriate specialty; grading accuracy refers to the triage nurse's ability to accurately distinguish the patient's condition into level 1 (critical), level 2 (severe), level 3 (urgent), and level 4 (non-urgent)<sup>[3]</sup>.

## 1.4 Statistical Methods

Using SPSS25.0 statistical software, measurement data are described by  $(\overline{x} \pm s)$  and tested with ttest; count data are described by rate and tested with  $\chi^2$  test or Fisher's exact probability method, P < 0.05 indicates a statistically significant difference.

## 2 Results

The pre-triage accuracy rate and grading accuracy rate of the experimental group were significantly higher than those of the control group (P < 0.05), as illustrated in Table 1. The triage assessment time for the experimental group was (2.14±0.80) minutes, shorter than that of the control group (2.89±0.98) minutes, with a significant difference (t = 3.562, P = 0.001).

## 3 Discussion

Currently, there is no unified standard for the triage of Acute Abdomen in clinical practice. Nurses mainly rely on their professional level and experience for triage, which involves a certain

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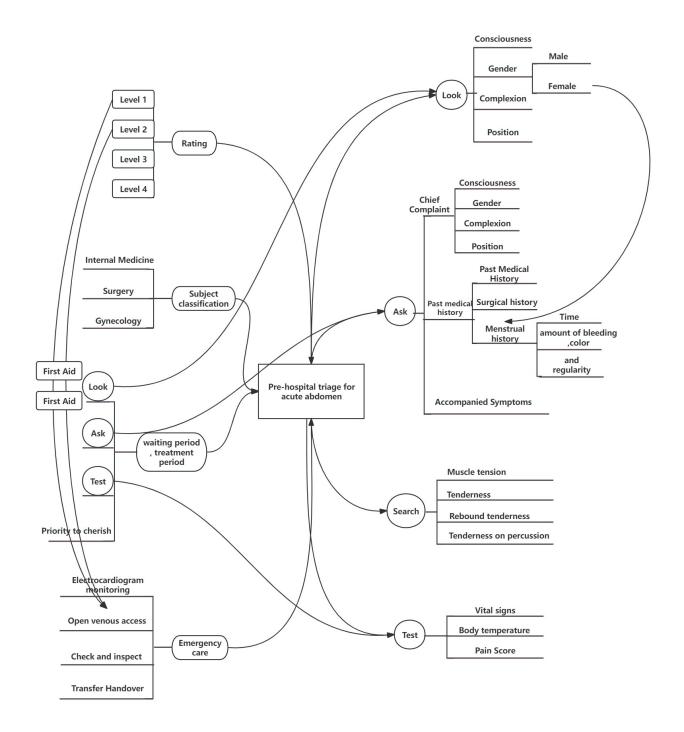


Figure 1: Mind Map for Acute Abdomen Triage

degree of subjectivity and uncertainty. This is especially true for patients with unclear symptoms, or for the elderly and children who may not fully describe their symptoms, leading to potential errors in departmental classification and grading by nurses, thereby missing the optimal treatment time<sup>[4]</sup>. Mind Map is a training tool that fully integrates reading and thinking, making it easy to follow patterns, allowing learners to quickly grasp the necessary information. It is currently widely used in nursing education, nursing management, and health education<sup>[5]</sup>.

This study applied mind maps to the pre-triage of acute abdomen cases. The mind map group created the mind maps through literature review, current situation analysis, and discussion to ensure the content was systematic and comprehensive. They continuously refined and modified the mind maps in clinical practice to ensure the feasibility of the designed mind maps<sup>[6]</sup>. The results indicated that the accuracy of pre-triage classification and grading in the experimental group was higher than that in the control group, demonstrating that mind maps can significantly enhance the accuracy of acute abdomen triage. The reason may be that the mind maps clearly present the key points of acute abdomen triage in graphic branches, which are well-organized. This can overcome the shortcomings of conventional emergency triage methods, where scattered inquiry language and unclear thinking lead to incomplete observation and inquiry of medical history. It avoids subjectivity and blindness in triage, quickly and intuitively guides the triage thinking of emergency nurses, and helps improve triage accuracy<sup>[7]</sup>.

In addition, this study also found that the triage time in the experimental group was significantly shorter than that in the control group. The reason is that the Mind Map can help emergency nurses quickly and proficiently master the triage process and emergency handling plan for Acute Abdomen. This allows them to make a quick and accurate preliminary judgment of the patient's condition when receiving patients with Acute Abdomen, thereby shortening the triage time<sup>[8]</sup>. At the same time, the Mind Map clarifies the key points of triaging Acute Abdomen for emergency nurses, effectively avoiding ineffective communication between nurses and patients, helping to reduce triage assessment time, and facilitating early treatment for patients.

In summary, the pre-triage process based on the Mind Map can significantly improve the accuracy and efficiency of triaging Acute Abdomen in emergency departments, achieving standardized management of Acute Abdomen triage, and is worth promoting.

### **Article History**

Received: July 10, 2024 Accepted: July 12, 2024 Published: September 30, 2024 References

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**To Cite This Article** Hebao SHU,et al. (2024). Research on the Application of Mind Map in Emergency Triage of Acute Abdomen. *Medical Research*, 6(3), 1-6. https://doi.org/10.6913/mrhk.060301

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

# Emergency treatment for a tetanus patient and literature review

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## Abstract

Tetanus is an acute zoonotic disease caused by the invasion of tetanus bacteria into wounds, where they proliferate and secrete toxins. This condition is characterized by persistent skeletal muscle spasms and heightened excitability of nerve reflexes, manifesting as clenched jaws and both tonic and clonic spasms. The primary muscle groups affected are the masseter, dorsal, abdominal, and limb muscles<sup>[1]</sup>. Key measures for treating tetanus include thorough wound management, as well as controlling muscle spasms and lung infections<sup>[2]</sup>. This article presents a case of tetanus, initially diagnosed in the internal medicine department. After excluding conditions related to stroke, the patient was transferred to the surgical department for debridement and anti-infection treatment. Ultimately, the patient's condition stabilized and showed improvement. We aim to deepen clinical physicians' understanding of tetanus by sharing the diagnostic and therapeutic insights from this case.

Keywords Tetanus; Muscle Spasms; Wound Management; Clostridium tetani; Immunization

## 1 Case Documentation

A 66-year-old male patient, weighing 52 kg, sought medical attention for unclear speech and restricted mouth opening that had persisted for 17 hours. The patient's family reported that 17 hours ago, they discovered the patient's speech was unclear, his mouth was restricted, and he was unable to extend his tongue, with symptoms progressively worsening. He also experienced discomfort during swallowing. There were no conscious disorders, hemiplegia, hemiblindness, or blurred vision. The patient did not report any discomfort such as fever, chills, chest tightness, chest pain, or cough. Initial consultation by a physician included cranial CT and MRI to rule out stroke. Upon further questioning regarding his medical history, it was revealed that the patient was accidentally injured by a wooden stick 12 days ago and did not receive proper treatment. Given the possibility of tetanus infection, he was transferred to the surgical department for continued diagnosis and treatment.

## 1.1 Physical Examination

- Body temperature: 36.5°C
- Pulse: 110 beats/min
- Respiration: 20 breaths/min
- Blood pressure: 162/100 mmHg

The patient was conscious with a wry smile on his face and tightly clenched jaws (Figure 1). Bilateral pupils were equal in size and round, measuring approximately 2.5 mm in diameter, and showed a sensitive response to light. There was no congestion in the conjunctiva and no cyanosis on the lips. Thoracic symmetry was noted, with coarse breath sounds in both lungs. No dry or wet rales were detected. The heart rhythm was regular, and no murmurs were identified in the heart valves. The abdomen was soft without tenderness or rebound pain. The limb muscle strength and tension were normal. The bilateral Babinski sign was negative, while neck resistance was positive. Visible swelling was evident at the distal end of the fourth finger on the left hand (Figure 2). Upon squeezing, purulent exudate was visible seeping from the nail bed.

## 1.2 Laboratory Results

- White blood cell count (WBC):  $11.13 \times 10^{9}$ /L
- Neutrophil percentage: 69%
- Red blood cell count (RBC):  $6.01 \times 10^{12}$ /L
- Platelet count (PLT): 315.00 × 10<sup>9</sup>/L
- Hypersensitive C-reactive protein: 4.07 mg/L

## 1.3 Liver and Kidney Function

• K+: 4.20 mmol/L



Figure 1. With clenched teeth and a bitter smile



Figure 3. Suppuration of nail bed



Figure 2. Swelling of finger



Figure 4. After debridement

- Na+: 137.68 mmol/L
- Creatinine (Cr): 99.17  $\mu$  mol/L
- Albumin (Alb): 45.57 g/L
- Alanine aminotransferase (ALT): 17.19 U/L

The emergency department reported the patient as critically ill. During treatment, the patient sweated profusely. After administering an intramuscular injection of 5000 IU tetanus immunoglobulin, the patient's condition improved. Partial debridement of the fingers was performed (Figures 3 and 4), along with local tetanus antitoxin injection therapy. Due to a positive penicillin skin test, cefuroxime and metronidazole were administered for anti-infection treatment. Fluid replacement, ECG monitoring, and oxygen therapy were provided for symptomatic treatment. Considering the patient had obvious muscle spasms, he was transferred to the ward for further treatment.

## 2 Discussion

#### 2.1 Overview of Tetanus

Tetanus is triggered by a neurotoxin produced by the *Clostridium tetani* bacterium, which enters the body through the skin or mucous membranes. The primary clinical symptom is muscle spasms. As the disease progresses, even mild stimuli can trigger generalized tonic seizures, resulting in numerous complications and potentially fatal outcomes <sup>[1]</sup>.

### 2.2 Global Impact

According to the 2016 Global Burden of Disease Study, the number of disability-adjusted life years (DALYs) for all ages due to tetanus globally in 2016 was 2.36 million, a decline of 90.5% compared to 1990<sup>[3]</sup>. The World Health Organization (WHO) asserts that the neonatal mortality rate from tetanus in 2010 was reduced by 93% compared to 1980<sup>[4]</sup>. However, for developing countries, tetanus is a pressing issue that demands serious attention. Although the incidence rate of tetanus in China is not clear, it occurs sporadically. The prevention of post-traumatic tetanus still faces issues such as the inappropriate use of tetanus toxoid and antitoxin, insufficient attention to active immunization, and non-standardized treatment of tetanus. In light of this case, the primary cause is the patient's inadequate awareness and insufficient emphasis on tetanus, coupled with a delay in seeking medical attention after the injury, ultimately resulting in wound infection and the development of tetanus.

#### 2.3 Pathogen Characteristics

The pathogen responsible for tetanus is *Clostridium tetani*, a member of the *Clostridium* genus, a Gram-positive, obligate anaerobe. Its spores are widely distributed within the soil and other environments. Although the incidence rate of tetanus is not high now, tetanus will pose a potential threat to public health when natural disasters occur. After the 2010 earthquake in Haiti, the incidence rate of tetanus was higher than usual, and the fatality rate of tetanus after serious natural disasters was between 19% and 31% <sup>[5]</sup>. *Clostridium tetani* can enter the human body through damaged skin, often due to wounds contaminated by objects such as soil, feces, sputum, punctures from nails or needles, burns, crush injuries, and injuries from fireworks and firecrackers, among others, with necrotic tissue inside the wound. There are also some less common routes of infection, such as epidermal wounds, surgical procedures, insect bites, tooth infections, open fractures, chronic wounds, and intravenous drug abuse. In a study of 2422 tetanus patients, 21.9% showed no obvious invasive wounds, implying that *Clostridium tetani* may enter the body via minor abrasions <sup>[6]</sup>. Similarly, according to the medical history, the patient in this case also did not have any obvious open wounds.

#### 2.4 Incubation Period and Clinical Categories

The incubation period for tetanus ranges from 3 to 21 days, typically around 10 days. However, varying with the wound's characteristics, size, and location, the period can extend from 1 day to several months. It has also been observed when removing foreign objects, such as shrapnel, that have been in the body for many years <sup>[7]</sup>. Tetanus is clinically categorized into three types: systemic tetanus (88%), local tetanus (12%), and head tetanus (1%) <sup>[8]</sup>. In this case, the patient exhibited a 10-day incubation period and displayed typical clinical symptoms at the time of consultation, fitting the systemic type. The shorter the incubation period, the less favorable the prognosis <sup>[9]</sup>. The bacterial cells themselves and exotoxins do not exhibit significant tissue toxicity at the local site, and there might not be any evident signs of inflammation or infection. Some wounds may even appear healed. In this case, the patient showed no open wounds upon presentation, yet local tissue swelling was noted.

#### 2.5 Immunity and Prevention

Tetanus spores are widely present in the natural environment, and humans generally have no natural immunity to tetanus. Therefore, artificial immunity is needed to make the body develop immunity to tetanus toxin. There are two methods: active immunity and passive immunity. Tetanus is a preventable disease because the growth of *Clostridium tetani* requires an anaerobic environment. Early and thorough debridement and improved circulation after trauma are key factors in preventing tetanus. Active immunity, also known as automatic immunity, involves injecting tetanus toxoids into the human body, causing the body to produce antibodies against tetanus toxin, thereby gaining immunity. Research has shown that three doses of tetanus basic immunity in infants and young children, combined with one dose of booster immunity in the second year, will provide 3-5 years of protection. Children can receive another dose of booster immunity in the early stages, and the protective effect can last until adolescence. If adolescents continue to receive one dose of booster immunity, it can provide long-term protection into adulthood, including for women of reproductive age <sup>[10]</sup>. The tetanus vaccine is safe for use, with a low incidence of adverse reactions.

#### 2.6 Passive Immunity

Passive immunity refers to the body's passive reception of tetanus toxin antibodies, which can confer immunity rapidly but for a limited duration. The commonly used passive immune drugs currently include refined tetanus antitoxin (TAT) injection, human tetanus immunoglobulin (HTIG), and equine tetanus immunoglobulin. TAT is a liquid antitoxin globulin preparation derived from TT-immunized horse plasma, refined through gastric enzyme digestion. It encompasses IgG from horse serum and necessitates a skin test prior to use, as it frequently induces allergic reactions. The prevalence of these reactions ranges from 5% to 30%, with an approximate fatality rate of 1 in 10,000 <sup>[11]</sup>. A literature analysis revealed that among 2636 patients experiencing adverse reactions to TAT, 10 fatalities occurred <sup>[12]</sup>. HTIG uses tetanus vaccine to immunize blood donors, collects plasma containing high-titer tetanus antibodies for purification, or uses gene recombination technology to prepare, with a low allergic reaction rate, high titer, long in vivo half-life (3-4 weeks), convenient use, and no need for skin testing <sup>[11, 13]</sup>. The market time of tetanus immunoglobulin is relatively short. The addition of column chromatography purification process reduces the content of IgG and other macromolecular proteins, increases the relative content of the active ingredient antibody fragment F(ab')2, and reduces allergy rates. It has been clinically used in some hospitals <sup>[14-16]</sup>. More clinical research is needed as a substitute for HTIG when it cannot be obtained, but skin tests are still required before use, using subcutaneous or intramuscular injections of 1500-3000U. The method for tetanus prophylaxis following trauma is determined by the type of injury and the individual's vaccination history. We need to pay attention to distinguishing between susceptible and non-susceptible tetanus wounds, identifying high-risk wounds, and inquiring about the victim's active immunization history.

## 2.7 Treatment Principles

The main principles of tetanus treatment include sedation, analgesia, muscle relaxation to control spasms, and correction of autonomic dysfunction to avoid exhaustion. Thorough debridement and anti-*Clostridium tetani* treatment; neutralizing toxins in the circulatory system; symptomatic and supportive treatment <sup>[17-19]</sup>. At present, the immunization coverage rate for children with tetanus is relatively high, but the immunity to tetanus decreases in adulthood. We call for attention to strengthening immunization for special populations, such as military personnel, police, construction workers, horticultural workers, farmers, field workers, and explorers, to enhance the adult immune barrier against tetanus. By reviewing case studies, summarizing the essentials of tetanus prevention and treatment, and incorporating the latest research, we aim to offer guidance for clinical diagnosis and treatment.

### **Article History**

Received: July 3, 2024 Accepted: July 10, 2024 Published: September 30, 2024 References

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- To Cite This Article Yutian LEI, et al. (2024). Emergency treatment for a tetanus patient and

literature review. Medical Research, 6(3), 7-14. https://doi.org/10.6913/mrhk.060302

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

## Clinical Effectiveness and Biochemical Impacts of Minimally Invasive versus Open Transforaminal Lumbar Interbody Fusion: A Meta-Analysis

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## Abstract

**Objective:** This meta-analysis aimed to compare the clinical effectiveness, safety, and biochemical impacts of two spinal surgery techniques: open transforaminal lumbar interbody fusion (open-TLIF) and minimally invasive TLIF (MIS-TLIF). **Methods:** A comprehensive literature search was conducted through April 2023 across PUBMED, Cochrane Library, SCOPUS, Web of Science, EMBASE, and CNKI, using the terms "transforaminal lumbar interbody fusion" or "TLIF" combined with "minimally invasive" or "open." A total of 44 studies met the inclusion criteria for analysis. **Results:** The meta-analysis found that MIS-TLIF results in higher intraoperative radiological exposure but less blood loss, lower postoperative drainage, shorter hospital stays, and better outcomes on the Visual Analog Scale (VAS) and Oswestry Disability Index (ODI). Biochemically, MIS-TLIF is associated with lower CRP, CK-MM, and CPK levels 24 hours post-operation compared to open TLIF. **Conclusions:** MIS-TLIF demonstrates superior clinical effectiveness, improved safety, and reduced muscle injury compared to open TLIF, making it a better option when minimizing tissue trauma and promoting rapid recovery are priorities.

Keywords Minimally Invasive Surgery (MIS), Transforaminal Lumbar Interbody Fusion (TLIF), Clinical Effectiveness, Biochemical Markers, Postoperative Recovery

**To Cite This Article** Jingyu LIU,et al. (2024). Clinical Effectiveness and Biochemical Impacts of Minimally Invasive versus Open Transforaminal Lumbar Interbody Fusion: A Meta-Analysis. *Medical Research*, 6(3), 15-39. https://doi.org/10.6913/mrhk.060303

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

## 1 Background

Lumbar fusion technology is extensively employed in managing lumbar instability and spinal deformities<sup>[1]</sup>. The primary objective is to restore the height of intervertebral discs and spinal segments, thereby alleviating nerve compression<sup>[2]</sup>. Since its initial description by Harms and Rolinger in 1982, TLIF has been performed using a single posterolateral approach to achieve circumferential fusion<sup>[3]</sup>. This technique, executed through a paramedian skin incision, allows transforaminal access with minimal neural retraction. The lateral trajectory offers significant benefits: (1) limited nerve retraction, reducing the risk of iatrogenic injury; (2) utilization of contralateral intact bony structures as additional fusion sites; and (3) potential for bilateral decompression without the morbidity associated with extensive contralateral soft tissue, muscle, and neural manipulation<sup>[4, 5]</sup>.

Despite the widespread adoption of TLIF, its associated challenges, such as muscle atrophy and scar formation due to the anatomical disruption of the paraspinal muscles, have been linked to long-term postoperative pain and disability<sup>[6]</sup>. These complications, along with prolonged hospital stays and high costs, remain significant drawbacks.

In recent years, MIS-TLIF has gained attention due to its smaller incision, reduced tissue damage, and faster recovery<sup>[7]</sup>. The procedure involves the insertion of a tubular retractor through a small incision, allowing the surgeon to operate without extensive muscle cutting. Damaged discs are removed to relieve pressure on the spinal cord or nerves, followed by the placement of an artificial spacer between vertebrae and stabilization with screws and rods to aid in spinal alignment during healing<sup>[8]</sup>. While the efficacy and safety of MIS-TLIF are increasingly recognized, its success depends on patient selection, severity of lumbar deformity, and pre-existing conditions such as spinal instability, sagittal imbalance, osteoporosis, and advanced bone loss, which may contraindicate lateral fusion approaches<sup>[9]</sup>. Furthermore, the learning curve associated with MIS-TLIF can lead to complications such as dural tears, implant misplacement, nerve damage, and incomplete fusion, necessitating enhanced surgical training<sup>[10]</sup>.

Given the inconsistent results from studies comparing the clinical outcomes and fusion rates of these techniques, our meta-analysis seeks to provide cumulative estimates of clinical efficacy and determine which surgical approach offers greater benefits.

## 2 Methods

## 2.1 A systematic search of the literature was conducted up to April 2023 across multiple databases

Including PUBMED, the Cochrane Library, SCOPUS, Web of Science, EMBASE, and CNKI. The search employed key terms such as "transforaminal lumbar interbody fusion" or "TLIF" alongside "minimally invasive" or "open". Additionally, reference lists of relevant studies were examined. No language restrictions were applied. This study adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the Methodological Quality of Systematic Reviews) guidelines<sup>[11]</sup>.

## 2.2 Studies were eligible for inclusion if they

(1) utilized a comparative design comparing MIS-TLIF with open TLIF; (2) involved adult patients with degenerative lumbar conditions such as disc herniation, spinal stenosis, or spondylolisthesis; (3) reported on perioperative outcomes such as operative time, blood loss, improvements in pain or disability, or fusion rates; and (4) included a follow-up period of at least six months post-surgery. If multiple studies from the same group met the inclusion criteria, outcomes were compared, and the most comprehensive or recent study was selected.

## 2.3 Exclusion criteria included literature reviews

Case reports, conference abstracts, editorials, biomechanical studies, animal studies, cadaver studies, and studies where full texts or data could not be retrieved were excluded.

## 2.4 Data Extraction and Quality Assessment: Data were extracted for each study

Including the first author's name, year of study, study design, patient demographics, and outcomes such as operative duration, blood loss, and hospital stay. The quality of the included studies was assessed by two independent reviewers (CZX and LJY) using the Newcastle-Ottawa Scale<sup>[12]</sup>. Although high-quality randomized controlled trials were scarce, the included studies (with NOS scores ranging from 5 to 9) are considered to have high methodological quality. However, there were notable limitations that may diminish the overall quality of evidence. These limitations include the small number of studies available for certain subgroup analyses, incomplete clinical outcome data in some studies, and two studies with small sample sizes that potentially increased heterogeneity and bias. Additionally, the restriction to studies published in English may have introduced language bias.

## 2.5 Statistical Analysis: Data analysis was performed using Review Manager

Clinical outcomes were analyzed as score differences between the 2-year follow-up and presurgery values. Mean differences (MD) and 95% confidence intervals (CI) were calculated for continuous variables, and relative risks (RR) for dichotomous variables. Heterogeneity was assessed using the Chi-squared (Cochrane Q) test and the I<sup>2</sup> statistic. A fixed-effects meta-analysis was applied if  $p \ge 0.1$  and I<sup>2</sup>  $\le 50\%$ ; otherwise, a random-effects model was used<sup>[13]</sup>. Strategies to address heterogeneity were implemented as outlined in the Cochrane Handbook<sup>[14]</sup>. All tests were two-sided, with statistical significance set at an alpha level of 0.05 unless otherwise specified.

## 3 Methods

Search Strategy and Inclusion Criteria: A systematic search of the literature was conducted up to April 2023 across multiple databases, including PUBMED, the Cochrane Library, SCOPUS,

Web of Science, EMBASE, and CNKI. The search employed key terms such as "transforaminal lumbar interbody fusion" or "TLIF" alongside "minimally invasive" or "open". Additionally, reference lists of relevant studies were examined. No language restrictions were applied. This study adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the Methodological Quality of Systematic Reviews) guidelines<sup>[11]</sup>.

Studies were eligible for inclusion if they: (1) utilized a comparative design comparing MIS-TLIF with open TLIF; (2) involved adult patients with degenerative lumbar conditions such as disc herniation, spinal stenosis, or spondylolisthesis; (3) reported on perioperative outcomes such as operative time, blood loss, improvements in pain or disability, or fusion rates; and (4) included a follow-up period of at least six months post-surgery. If multiple studies from the same group met the inclusion criteria, outcomes were compared, and the most comprehensive or recent study was selected.

Exclusion criteria included literature reviews, case reports, conference abstracts, editorials, biomechanical studies, animal studies, cadaver studies, and studies where full texts or data could not be retrieved.

Data Extraction and Quality Assessment: Data were extracted for each study, including the first author's name, year of study, study design, patient demographics, and outcomes such as operative duration, blood loss, and hospital stay. The quality of the included studies was assessed by two independent reviewers (CZX and LJY) using the Newcastle-Ottawa Scale<sup>[12]</sup>. Although high-quality randomized controlled trials were scarce, the included studies (with NOS scores ranging from 5 to 9) are considered to have high methodological quality. However, there were notable limitations that may diminish the overall quality of evidence. These limitations include the small number of studies available for certain subgroup analyses, incomplete clinical outcome data in some studies, and two studies with small sample sizes that potentially increased heterogeneity and bias. Additionally, the restriction to studies published in English may have introduced language bias.

Statistical Analysis: Data analysis was performed using Review Manager (version 5.3). Clinical outcomes were analyzed as score differences between the 2-year follow-up and pre-surgery values. Mean differences (MD) and 95% confidence intervals (CI) were calculated for continuous variables, and relative risks (RR) for dichotomous variables. Heterogeneity was assessed using the Chi-squared (Cochrane Q) test and the I<sup>2</sup> statistic. A fixed-effects meta-analysis was applied if  $p \ge 0.1$  and I<sup>2</sup>  $\le 50\%$ ; otherwise, a random-effects model was used<sup>[13]</sup>. Strategies to address heterogeneity were implemented as outlined in the Cochrane Handbook<sup>[14]</sup>. All tests were twosided, with statistical significance set at an alpha level of 0.05 unless otherwise specified.

## 4 Results

#### 4.1 Literature Survey

Our systematic search identified 44 studies, as detailed in Table 1. The initial search strategy yielded 87 records. After screening the titles and abstracts, 64 articles remained. Seventeen studies

were excluded due to duplication, meta-analysis overlaps, technical indications, commentaries, and cadaveric studies. Ultimately, 44 studies met the inclusion criteria after a full-text review (Figure 1).

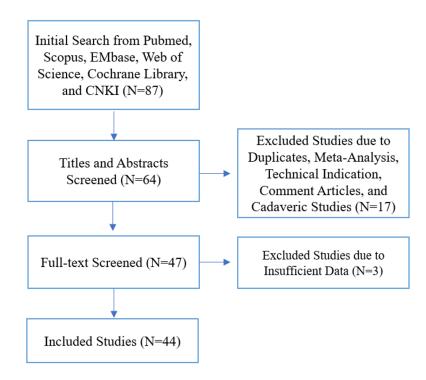


Figure 1: Flowchart

Intraoperative Radiological Exposure: In a meta-analysis of 12 studies involving 1,394 patients, the weighted mean difference (WMD) in intraoperative radiological exposure time favored the open group, with the minimally invasive surgery (MIS) group experiencing an average of 30.97 seconds longer exposure (95% CI: 20.53 to 41.42, P < 0.00001). This result was accompanied by substantial heterogeneity (I<sup>2</sup> = 99%, Figure 2).

		MS		(	Dpen			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Tota	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
Chan Weam Benedict Peng. 2009	105.5	17.5	29	35.2	6.25	29	8.2%	70.30 [63.54, 77.06]	
Chusheng seng et al. 2013	55.2	11.3	40	16.4	2.1	40	8.4%	38.80 [35.24, 42.36]	
Kong et al. 2012	49	33.5	72	17.6	20	72	8.0%	31.40 [22.39, 40.41]	
Li Ming 2016	15	7	19	11	5	34	8.4%	4.00 [0.43, 7.57]	· ·
Tang FuXing 2015	18.7	8.9	28	6.9	2.3	30	8.4%	11.80 [8.40, 15.20]	· ·
Wang Hong Li 2011	92.7	13.8	41	43	10.2	38	8.3%	49.70 [44.37, 55.03]	
Wang Jian 2011	51	19	172	20	10	199	8.4%	31.00 [27.84, 34.16]	
Xu Hui 2013	52.3	21.4	48	21.5	11.8	48	8.2%	30.80 [23.89, 37.71]	
Yang Jin 2013	75	19	43	22	6	104	8.3%	53.00 [47.21, 58.79]	
Yang Yang 2015	59.8	4.8	50	22.4	3.4	50	8.5%	37.40 [35.77, 39.03]	
Zhang Hai Long 2011	18.2	9.2	23	5.1	2.3	26	8.4%	13.10 [9.24, 16.96]	
Zhang Wen Zhi 2013	30	8	82	28	10	76	8.4%	2.00 [-0.84, 4.84]	*
Total (95% CI)			647			746	100.0%	30.97 [20.53, 41.42]	•
Heterogeneity: Tau <sup>2</sup> = 334.31; ChF =	= 1093.6	4. df =	11 (P •	< 0.0000	)1); I <sup>2</sup> :	= 99%			
Test for overall effect: Z = 5.81 (P <									-100 -50 0 50 100 Favours (experimental) Favours (control)

Figure 2: Intraoperative radiological exposure

## 4.2 Blood Loss

Analysis of 39 studies comprising 3,276 patients revealed significantly greater blood loss in the open group compared to the MIS group, with a WMD of 230.55 ml (95% CI: -273.92 to -187.19, P < 0.00001), also demonstrating high heterogeneity (I<sup>2</sup> = 98%, Figure 3).

		MIS			Open			Mean Difference	Mean Difference
Study or Subgroup	Mean		Total	Mean		Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Alan T.Villavicencio 2011	163	131.2	76	366.8	298.2	63	2.5%	-203.80 [-283.12, -124.48]	
Chan Weam Benedict Peng. 2009	150	100	29	681	250	29	2.4%	-531.00 [-629.00, -433.00]	
Chu Ya Wei 2014	362	166	15	590	135	36		-228.00 [-322.88, -133.12]	
Chusheng seng et al. 2013	127.3	45.7	40	405	80	40		-277.70 [-306.25, -249.15]	-
Dhall SS 2008	194	182.8	21	505	182.8	21	2.4%	-311.00 [-421.57, -200.43]	
F. Zairi 2013	148	488	40	486	488	60	1.8%	-338.00 [-533.24, -142.76]	
Giovanni B 2015	230	50	30	620	112.5	34	2.7%	-390.00 [-431.83, -348.17]	
Hwee Weng Dennis Hey 2015	237.4	57.5	21	251.1	65.6	21	2.7%	-13.70 [-51.01, 23.61]	-+
Jason S. Cheng 2013	392.5	284	50	535.5	324	25	2.1%	-143.00 [-292.42, 6.42]	
Jian Guan 2016	120.2	63.7	44	306.5	165.7	54	2.7%	-186.30 [-234.34, -138.26]	-
Jian Wang 2010	264	89	42	673	145	43	2.7%	-409.00 [-460.02, -357.98]	
Kern et al. 2014	124.4	92	33	380.3	191.2	33	2.6%	-255.90 [-328.29, -183.51]	
Kong et al. 2012	50.6	161	72	447.4	519.2	72	2.3%	-396.80 [-522.36, -271.24]	
Kriangsak Saetia 2013	317	195.79	12	645.85	451.99	12	1.3%	-328.85 [-607.54, -50.16]	
Li Ming 2016	125	166	19	460	135	34	2.5%	-335.00 [-422.35, -247.65]	
Li Yu 2015	259.67	20.34	33	347.06	16.83	37	2.8%	-87.39 [-96.20, -78.58]	•
Liang Bo Wei 2011	193.8	86.2	42	357.2	116.4	45	2.7%	-163.40 [-206.25, -120.55]	
Luo Zhi Ping 2015	175	56	42	296	108	54	2.7%	-121.00 [-154.42, -87.58]	-
Miguel et al. 2012	125	76.3	33	274.6	99.4	33	2.7%	-149.60 [-192.35, -106.85]	-
Owoicho et al. 2011	218.8	37.7	15	305	21	15	2.8%	-86.20 [-108.04, -64.36]	· •
QI QiHua 2015.	200.4	70.57	28	260.54	100.34	26	2.7%	-60.14 [-106.73, -13.55]	
Shu Dong Ping 2016	367	72	26	92.1	88	26	2.7%	274.90 [231.20, 318.60]	
Shunwu, Fan 2010	399.8	125.8	32	517	147.8	30	2.6%	-117.20 [-185.73, -48.67]	
Tang FuXing 2015	245.8	56	28	394.2	92.1	30	2.7%	-148.40 [-187.34, -109.46]	
Tang Hongwei 2016	202.5	148.2	20	482	199.9	25	2.4%	-279.50 [-381.28, -177.72]	
Wale et al.2014	95	20	57	786	107	11	2.6%	-691.00 [-754.44, -627.56]	
Wang Hong Li 2011	207.7	57.6	41	258.9	122.2	38	2.7%	-51.20 [-93.87, -8.53]	
Wang Jian 2011	310	75	172	623	156	199	2.8%	-313.00 [-337.40, -288.60]	
Wang Lin Jie 2015	56.3	23.2	43	167.4	47.5	43	2.8%	-111.10 [-126.90, -95.30]	
Xu Hui 2013	211.5	45.8	48	534.6	100.4	48	2.7%	-323.10 [-354.32, -291.88]	-
Yan XiongWei 2016	482.8	274.8	51	787.9	264.7	46		-305.10 [-412.52, -197.68]	
Yang Jin 2013	362	177	43	720	171	104	2.6%	-358.00 [-420.28, -295.72]	
Yang Lin 2014	355	89	35	588	152	35	2.7%	-233.00 [-291.35, -174.65]	
Yang Yang 2015	183.9	24.2	50	490.7	75.3	50	2.8%	-306.80 [-328.72, -284.88]	×
You Lv 2017	143.1	37.4	50	289.7	77.4	56	2.8%	-146.60 [-169.37, -123.83]	
Zhang Hai Long 2011	203.6	57.4	23	513.8	219.4	26		-310.20 [-397.73, -222.67]	
Zhang Wen Zhi 2013	250	75	82	650	150	76		-400.00 [-437.43, -362.57]	
Zheng Yang 2014	198.6	81.6	22	350	143.6	26	2.6%	-151.40 [-216.28, -86.52]	
Zhou Shu 2013	131.3	74.1	30	318.3	177.4	30	2.6%	-187.00 [-255.80, -118.20]	
Total (95% CI)			1590			1686	100.0%	-230.55 [-273.92, -187.19]	•
Heterogeneity: Tau <sup>2</sup> = 17579.26; Ch	i <sup>2</sup> = 2134.	53, df = 3	38 (P <	0.000013	; I <sup>z</sup> = 989	%			
Test for overall effect: Z = 10.42 (P <									-500 -250 0 250 500 Favours [experimental] Favours [control]

Figure 3: Intraoperative blood loss.

## 4.3 Postoperative Drainage Volume

Data from 15 studies, including 1,488 patients, indicated that postoperative drainage volume was significantly less in the MIS group by 103.76 ml (95% CI: -125.15 to -82.38, P < 0.00001), with notable heterogeneity observed (I<sup>2</sup> = 94%, Figure 4).

## 4.4 Surgery Time

Despite evidence of substantial heterogeneity, there were no significant differences in surgery time between the MIS and open groups across 40 studies involving 3,470 patients ( $I^2 = 99\%$ , Figure 5).

		MIS		(	Open			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Tota	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Chu Ya Wei 2014	72	34	15	120	71	36	6.7%	-48.00 [-76.88, -19.12]	
Jian Wang 2010	39	12	42	158	65	43	7.2%	-119.00 [-138.76, -99.24]	-
Li Yu 2015	29.64	4.35	33	134.72	25.68	37	7.5%	-105.08 [-113.49, -96.67]	-
Liang Bo Wei 2011	113.5	57.6	42	227.5	88.1	45	6.6%	-114.00 [-145.08, -82.92]	
Luo Zhi Ping 2015	67	19	42	154	62	54	7.2%	-87.00 [-104.51, -69.49]	
QI QiHua 2015.	153.27	43.51	28	203.46	67.31	26	6.6%	-50.19 [-80.67, -19.71]	
Shu Dong Ping 2016	71	33	26	122	50	26	7.0%	-51.00 [-74.03, -27.97]	
Shunwu, Fan 2010	178.2	75.2	32	194.4	79.3	30	6.1%	-16.20 [-54.72, 22.32]	
Tang FuXing 2015	141.6	53.3	28	253.3	77.8	30	6.4%	-111.70 [-145.83, -77.57]	
Wang Hong Li 2011	114.6	53.1	41	266.6	80	38	6.6%	-152.00 [-182.19, -121.81]	
Wang Jian 2011	38	12	172	184	72	199	7.5%	-146.00 [-156.16, -135.84]	~
Yang Jin 2013	61	33	43	192	73	104	7.3%	-131.00 [-148.15, -113.85]	
Yang Lin 2014	80	21	35	121	52	35	7.2%	-41.00 [-59.58, -22.42]	
Zhang Wen Zhi 2013	50	15	82	200	75	76	7.3%	-150.00 [-167.17, -132.83]	
Zheng Yang 2014	115.7	74.5	22	494.7	243.9	26	2.9%	-379.00 [-477.78, -280.22]	•
Total (95% CI)			683			805	100.0%	-103.76 [-125.15, -82.38]	◆
Heterogeneity: Tau <sup>2</sup> =	1562.52	$Chi^2 = 2$	53.02	df = 14 (F	< 0.00	1001): P			
Test for overall effect: 2	•								-200 -100 0 100 200 Favours (experimental) Favours (control)

Figure 4: Postoperative drainage volume.

		MS			Open			Mean Difference	Mean Difference
study or Subgroup	Mean	SD	Tota	Mean	SD	Tota	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Van T.Villavicencio 2011	222.5	67.5	76	214.9	60	63	2.5%	7.60 [-13.61, 28.81]	- <del>-</del> -
Chan Weam Benedict Peng. 2009	216.4	60	29	170.5	40	29	2.4%	45.90 [19.65, 72.15]	
Chu Ya Wei 2014	163	30	15	170	25	36	2.5%	-7.00 [-24.24, 10.24]	-
Chusheng seng et al. 2013	185	8.7	40	166	7	40	2.6%	19.00 [15.54, 22.46]	
Dhall SS 2008	199	60.1	21	237	60.1	21	2.3%	-38.00 [-74.35, -1.65]	
7. Zairi 2013	170	39.5	40	186	39.5	60	2.5%	-16.00 [-31.80, -0.20]	-
Giovanni B 2015	144	33	30	102	28.5	34	2.5%	42.00 [26.79, 57.21]	-
lwee Weng Dennis Hey 2015	269	40.7	21	187	54.9	21	2.4%	82.00 [52.77, 111.23]	1.000
ason S. Cheng 2013	244.6	73	50	278.8	14.5	25	2.5%	-34.20 [-55.22, -13.18]	~
lian Guan 2016	329.3	69.3	44	234.9	67.4	54	2.4%	94.40 [67.15, 121.65]	
lian Wang 2010	156	32	42	145	27	43	2.6%	11.00 [-1.60, 23.60]	· ·
Kern et al. 2014	115.8	28.2	33	186	31	33	2.5%	-70.20 [-84.50, -55.90]	-
Kong et al. 2012	166.4	52.1	72	181.8	45.4	72	2.5%	-15.40 [-31.36, 0.56]	7
<riangsak 2013<="" saetia="" td=""><td>340</td><td>81.49</td><td>12</td><td>324</td><td>107.45</td><td>12</td><td>1.7%</td><td>16.00 [-60.30, 92.30]</td><td></td></riangsak>	340	81.49	12	324	107.45	12	1.7%	16.00 [-60.30, 92.30]	
i Ming 2016	195	45	19	154	32	34	2.5%	41.00 [18.08, 63.92]	
Li Yu 2015	145.38	13.48	33	139.61	12.55	37	2.6%	5.77 [-0.35, 11.89]	r
iang Bo Wei 2011.	126.5	59.7	42	95.6	45.8	45	2.5%	30.90 [8.43, 53.37]	~
uo Zhi Ping 2015	96	37	42	83	25	54	2.6%	13.00 [-0.03, 26.03]	-
liguel et al. 2012	112	36.7	33	184.6	33.8	33	2.5%	-72.60 [-89.62, -55.58]	-
Dwoicho et al. 2011	340	73	15	202.5	26.3	15	2.3%	137.50 [98.23, 176.77]	
QI QiHua 2015.	82.37	17.91	28	105.62	27.33	26	2.6%	-23.25 [-35.67, -10.83]	· · ·
3hu Dong Ping 2016	164	20	26	172	23	26	2.6%	-8.00 [-19.72, 3.72]	-
Shunwu, Fan 2010	159.2	21.7	32	142.8	22.5	30	2.6%	16.40 [5.38, 27.42]	-
ang FuXing 2015	198.1	16	28	147.9	23	30	2.6%	50.20 [40.06, 60.34]	· ·
ang Hongwei 2016	164.5	33.8	20	149.2	23.8	25	2.5%	15.30 [-2.21, 32.81]	
Vale et al.2014	161	7.6	57	375	14	11	2.6%	-214.00 [-222.51, -205.49]	*
Vang Hong Li 2011	168.7	36.4	41	145	26.8	38	2.5%	23.70 [9.67, 37.73]	-
Vang Jian 2011	132	29	172	145	37	199	2.6%	-13.00 [-19.72, -6.28]	
Vang Lin Jie 2015	131.4	38.6	43	102.6	22.7	43	2.6%	28.80 [15.42, 42.18]	+
(u Hui 2013	120.5	36.8	48	100.6	32.4	48	2.5%	19.90 [6.03, 33.77]	-
an XiongWei 2016	148.8	24.2	51	191.7	37.6	46	2.6%	-42.90 [-55.63, -30.17]	+
/ang Jin 2013	175	35	43	177	30	104	2.6%	-2.00 [-13.94, 9.94]	+
/ang Lin 2014	125	15	35	123	25	35	2.6%	2.00 [-7.66, 11.66]	+
/ang Yang 2015	178.5	17.7	50	146.3	18.8	50	2.6%	32.20 [25.04, 39.36]	*
/i-bing Li 2015	164.8	9.2	95	116	23.6	79	2.6%	48.80 [43.28, 54.32]	,
/ou Lv 2017	103.2	16.9	50	130.5	17.9	56	2.6%	-27.30 [-33.93, -20.67]	*
Zhang Hai Long 2011	128.5	39	23	104.3	46.1	26	2.5%	24.20 [0.37, 48.03]	h
Zhang Wen Zhi 2013	120.5	35	82	115	28	76	2.5%	5.00 [-4.85, 14.85]	÷
Zheng Yang 2014	235.8	46.3	22	127.8	45.8	26	2.4%	108.00 [81.84, 134.16]	
Zhou Shu 2013	149.5	40.9	30	175.2	37.3	30	2.4%	-25.70 [-45.51, -5.89]	-
			4005			4705	400.00		
fotal (95% CI) Isteragonaity: Tauž - 2042-20: Obiž	- 2054 4	E df = 1	1685	0.00004	12 - 000		100.0%	7.05 [-9.78, 23.88]	· · · · · · · · · · · · · · · · · · ·
leterogeneity: Tau² = 2842.30; Chi²	= 3004.4	o, ur = s	9 (P <	0.00001)	1.1.= 988	70			-500 -250 0 250

Figure 5: Surgery time comparison between MIS and open groups.

## 4.5 Length of Hospitalization

In 22 studies, including data from 15 studies that specifically compared the two groups, the MIS group demonstrated a shorter hospital stay by an average of 1.95 days compared to the open group (95% CI: -2.56 to -1.33, P < 0.00001). Significant heterogeneity was present in these findings (I<sup>2</sup> = 96%, Figure 6).

		MIS			Open			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Alan T.Villavicencio 2011	3	2.3	76	4.2	3.5	63	4.9%	-1.20 [-2.21, -0.19]	<b>_</b>
Chan Wearn Benedict Peng. 2009	4	1.25	29	6.7	1.6	29	5.2%	-2.70 [-3.44, -1.96]	
Chusheng seng et al. 2013	3.6	0.3	40	5.9	0.4	40	5.6%	-2.30 [-2.45, -2.15]	-
Giovanni B 2015	4.1	1	30	7.4	2.5	34	5.0%	-3.30 [-4.21, -2.39]	_ <b>-</b>
HeYong 2017	8.71	1.68	24	8.23	1.5	24	5.0%	0.48 [-0.42, 1.38]	
Hwee Weng Dennis Hey 2015	6.6	1	21	7	1.4	21	5.2%	-0.40 [-1.14, 0.34]	-++
Jason S. Cheng 2013	4.8	1.8	50	6.05	1.8	25	5.1%	-1.25 [-2.11, -0.39]	_ <b>—</b>
Jian Guan 2016	5	1.3	44	3.8	1.3	54	5.4%	1.20 [0.68, 1.72]	
Jian Wang 2010	10.6	2.5	42	14.6	3.8	43	4.4%	-4.00 [-5.36, -2.64]	
Kern et al. 2014	2.3	1.2	33	2.9	1.1	33	5.4%	-0.60 [-1.16, -0.04]	
Kong et al. 2012	3.2	2.9	72	6.8	3.4	72	4.9%	-3.60 [-4.63, -2.57]	<u> </u>
Kriangsak Saetia 2013	8.42	3.34	12	8.33	6.72	12	1.5%	0.09 [-4.16, 4.34]	
Li Yu 2015	7.52	1.34	33	9.96	2.21	37	5.1%	-2.44 [-3.29, -1.59]	<b>—</b>
Miguel et al. 2012	2	6.7	33	3	1.1	33	3.1%	-1.00 [-3.32, 1.32]	
Owoicho Adogwa 2012	3.19	0.24	14	3.875	0.161	7	5.6%	-0.69 [-0.86, -0.51]	+
Shu Dong Ping 2016	5	1	26	7	1	26	5.4%	-2.00 [-2.54, -1.46]	
Shunwu, Fan 2010	9.3	2.6	32	12.5	1.8	30	4.8%	-3.20 [-4.31, -2.09]	<u> </u>
Tang FuXing 2015	6.6	1.6	28	9.8	1.9	30	5.0%	-3.20 [-4.10, -2.30]	_ <b>—</b>
Wale et al.2014	3.6	1	57	3.2	0.2	11		Not estimable	
Nang Lin Jie 2015	6.5	3.2	43	8.3	4.6	43	4.0%	-1.80 [-3.47, -0.13]	
Yan XiongWei 2016	4.8	1.7	51	11.2	3.1	46	4.9%	-6.40 [-7.41, -5.39]	<u>→</u>
You Lv 2017	5.4	2.8	50	7.1	3.3	56	4.7%	-1.70 [-2.86, -0.54]	
Total (95% CI)			783			758	100.0%	-1.95 [-2.56, -1.33]	◆
Heterogeneity: Tau <sup>2</sup> = 1.74; Chi <sup>2</sup> = 5	03.81, df	= 20 (	P < 0.0	0001); F	<sup>2</sup> = 96%				
Test for overall effect: Z = 6.22 (P < 0		(							-4 -2 0 2 4
									Favours [experimental] Favours [control]

Figure 6: Length of hospitalization comparison between MIS and open groups.

### 4.6 Pain Outcomes Assessed by Visual Analog Scale (VAS)

#### 4.6.1 Short-term Follow-up ( $\leq 6$ Months)

Data from 12 studies analyzing VAS scores for back pain demonstrated that the minimally invasive surgery (MIS) group reported significantly lower pain scores compared to the open group, with a weighted mean difference (WMD) of -0.63 points (95% CI: -0.95 to -0.31, P = 0.001), accompanied by substantial heterogeneity (I<sup>2</sup> = 92%). Additionally, VAS scores for leg pain, derived from 8 studies, showed a reduction of 0.49 points in the MIS group (WMD = -0.49; 95% CI: -0.82 to -0.19, P = 0.004), with notable heterogeneity (I<sup>2</sup> = 88%).

### 4.6.2 One-year Follow-up

Analysis of 8 studies on VAS scores for back pain at one year revealed that the MIS group experienced a further reduction in pain by 0.37 points (WMD = -0.37; 95% CI: -0.62 to -0.13, P = 0.003), with persistent high heterogeneity (I<sup>2</sup> = 93%). For leg pain at the same follow-up interval, data from 5 studies indicated no statistically significant differences between the MIS and

open groups (WMD = -0.02; 95% CI: -0.12 to 0.09, P = 0.77), with moderate heterogeneity (I<sup>2</sup> = 41%, Figure 7).

#### 4.7 Long-term Pain Outcomes Assessed by Visual Analog Scale (VAS)

#### 4.7.1 Two-Year Follow-up

In a meta-analysis of 13 studies evaluating back pain, the minimally invasive surgery (MIS) group demonstrated a statistically significant reduction in pain scores compared to the open group, with a weighted mean difference (WMD) of -0.31 points (95% CI: -0.44 to -0.17, P < 0.00001). This finding was associated with moderate heterogeneity (I<sup>2</sup> = 73%). For leg pain assessed at the same two-year follow-up, data from 8 studies indicated no statistically significant differences between the MIS and open groups, with a WMD of -0.10 (95% CI: -0.25 to 0.06, P = 0.21). This outcome also displayed moderate heterogeneity (I<sup>2</sup> = 54%, Figure 7).

#### 4.8 Functional Outcomes as Assessed by the Oswestry Disability Index (ODI)

#### 4.8.1 Short-Term and Long-Term Follow-Up

Functional outcomes were evaluated using the ODI, a measure of disability due to back pain. At the one-month follow-up, data from 5 studies indicated that the minimally invasive surgery (MIS) group reported significantly lower disability scores compared to the open group, with a weighted mean difference (WMD) of -3.21 points (95% CI: -4.65 to -1.77, P < 0.0001). High heterogeneity was observed (I<sup>2</sup> = 95%).

At six months, 11 studies reported a continued advantage for the MIS group, with a WMD of -0.79 points (95% CI: -1.21 to -0.37), also accompanied by significant heterogeneity (I<sup>2</sup> = 96%).

At the one-year mark, 14 studies demonstrated that the MIS group maintained improved functional outcomes, with a WMD of -1.18 points (95% CI: -1.58 to -0.77), indicating substantial heterogeneity ( $I^2$  = 85%, Figure 8). Over a longer term, the two-year follow-up data from 20 studies showed that the MIS group's disability scores were consistently lower by 1.01 points (WMD = -1.01; 95% CI: -1.34 to -0.67), with moderate heterogeneity ( $I^2$  = 72%, Figure 8).

#### 4.9 Fusion Rates

Fusion success at grade 1 and grade 2 levels was assessed as a satisfactory outcome for lumbar fusion surgery. Analysis of the 6-month and 2-year fusion rates revealed no significant differences between the minimally invasive surgery (MIS) and open groups. At 6 months, the odds ratio (OR) was 0.90 (95% CI: 0.57 to 1.42, P = 0.65), and at 2 years, the OR was 0.86 (95% CI: 0.54 to 1.38, P = 0.54), with an overall effect showing an OR of 0.88 (95% CI: 0.64 to 1.22, P = 0.45). Chi-squared tests confirmed the absence of heterogeneity (I<sup>2</sup> = 0%, P = 0.83; Figure 9).

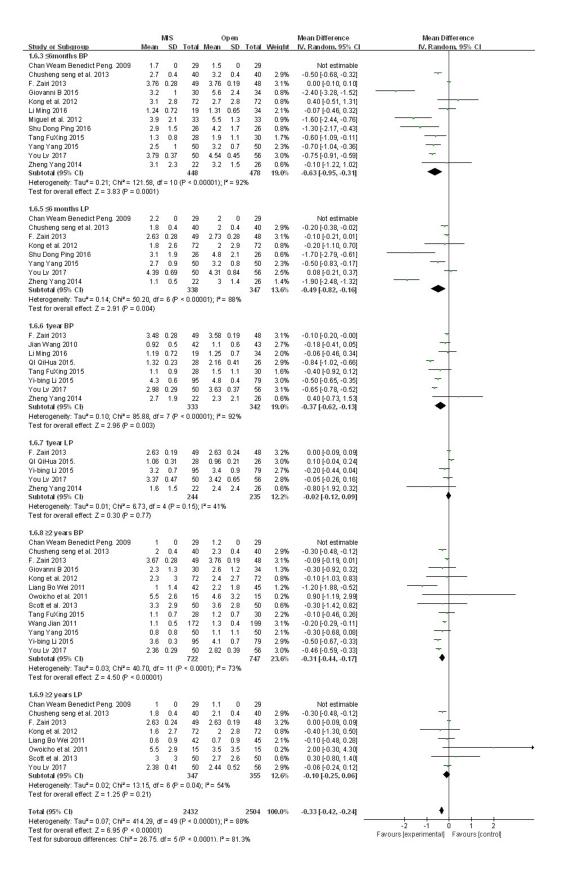


Figure 7: VAS scores comparison between MIS and open groups at different follow-up intervals.

#### 4.10 Physical and Mental Component Scores

Physical component scores from four studies indicated that the MIS group scored on average 3.21 points higher than the open group (WMD = 3.21, 95% CI: 0.03 to 6.40, P = 0.05). In contrast,

Study or Subgroup		MIS	Total		Open sp	Total	Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference
<u>Study or Subgroup</u> 1.7.1 ODI 1month	Mean	50	rota	Medil	50	rotal	weight	IV, FIXed, 95% CI	IV, Fixed, 95% CI
	10	6.1	20	22	10.5	24	0.204	14.00 [ 10.15 0.05]	
Giovanni B 2015	18	6.1	30	32	10.5	34		-14.00 [-18.15, -9.85]	
Li Yu 2015	34.24	4.36	33	38.62	4.23	37	1.2%	-4.38 [-6.40, -2.36]	ALC: MALERAL STREET
Luo Zhi Ping 2015	24.2	11.4	42	12.9	9.9	54	0.3%	11.30 [6.96, 15.64]	10 M - 10 M
Yang Yang 2015	29.2	10.2	50	33.6	10	50	0.3%	-4.40 [-8.36, -0.44]	
Zheng Yang 2014	23.9	6.4	22	23.7	7.5	26	0.3%	0.20 [-3.73, 4.13]	
Subtotal (95% CI)			177			201	2.3%	-3.21 [-4.65, -1.77]	•
Heterogeneity: Chi <sup>2</sup> = 73.38, df = 4 (	(P < 0.000	001); I <sup>2</sup> :	= 95%						
Test for overall effect: $Z = 4.38$ (P <	0.0001)								
1.7.2 6 months									
Chan Weam Benedict Peng. 2009	18.2	3.3	29	19.7	3.7	29	1.5%	-1.50 [-3.30, 0.30]	
Chusheng seng et al. 2013	21.5	2.5	40	23	2.8	40	3.5%	-1.50 [-2.66, -0.34]	
F. Zairi 2013	29.4	1.4	40	28	1.4	60	15.2%	1.40 [0.84, 1.96]	+
Kong et al. 2012	24.6	18.2	72	20.6	17.2	72	0.1%	4.00 [-1.78, 9.78]	
Li Yu 2015	29.75	4.18	33	33.17	2.4	37	1.8%	-3.42 [-5.04, -1.80]	
Shunwu, Fan 2010	20.5	8.7	32	24.4	10	30	0.2%	-3.90 [-8.58, 0.78]	
	20.5		28	31.6	9.7	30			
Tang FuXing 2015		8.6					0.2%	-7.00 [-11.71, -2.29]	
Wale et al.2014	26.4	0	57	41.2	0	11		Not estimable	
Wang Hong Li 2011	12	3	41	20	3	38	2.7%	-8.00 [-9.32, -6.68]	
Xu Hui 2013	14.2	4.3	48	18.7	5.8	48	1.1%	-4.50 [-6.54, -2.46]	
Zheng Yang 2014	9.5	6.3	22	9.6	5.7	26	0.4%	-0.10 [-3.53, 3.33]	
Subtotal (95% CI)			442			421	26.8%	-0.79 [-1.21, -0.37]	•
Heterogeneity: Chi≆ = 208.60, df = 9 Test for overall effect: Z = 3.66 (P =		0001); I <sup>a</sup>	e 96%	6					
1.7.3 ODI 1 year									
	14.00	~ ~	45	10.00	2.50	00	4 400	20 0 0 1 1 0 0 0 0 0	
Chu Ya Wei 2014	14.26	3.3		13.83	2.53	36	1.4%	0.43 [-1.43, 2.29]	
F. Zairi 2013	28	2.1	40	28	1.4	60	8.7%	0.00 [-0.74, 0.74]	T
HeYong 2017	28.5	3.02	24	25.46	3.19	24	1.5%	3.04 [1.28, 4.80]	
Jian Wang 2010	10.8	3.3	42	12.2	3.9	43	2.0%	-1.40 [-2.93, 0.13]	
Li Ming 2016	13.01	3.15	19	12.28	2.51	34	1.8%	0.73 [-0.92, 2.38]	
QI QiHua 2015.	9.57	1.42	28	13.25	3.22	26	2.6%	-3.68 [-5.02, -2.34]	
Shunwu, Fan 2010	22.5	9.7	32	26.2	9.3	30	0.2%	-3.70 [-8.43, 1.03]	
Tang FuXing 2015	22.7	9.3	28	26.2	10.5	30	0.2%	-3.50 [-8.60, 1.60]	
Tang Hongwei 2016	7.6	5.7	20	8.6	5.3	25	0.5%	-1.00 [-4.25, 2.25]	
Wang Hong Li 2011	10	2	41	13	2	38	6.1%	-3.00 [-3.88, -2.12]	-
	45.4	7.8	95	50.9	6.8	79	1.0%		
Yi-bing Li 2015 Zhang Haillang 2011								-5.50 [-7.67, -3.33]	
Zhang Hai Long 2011 Zhang Wan Zhi 2012	15.3	4.3	23	16.1	6.8	26	0.5%	-0.80 [-3.95, 2.35]	
Zhang Wen Zhi 2013	13.8	4.8	82	14.5	5.3	76	1.9%	-0.70 [-2.28, 0.88]	
Zheng Yang 2014	7.1	6	22	7.9	7.9	26	0.3%	-0.80 [-4.74, 3.14]	
Subtotal (95% CI)			511			553	28.7%	-1.18 [-1.58, -0.77]	•
Heterogeneity: Chi² = 87.17, df = 13 Test for overall effect: Z = 5.66 (P ≺		0001); I <sup>s</sup>	'= 85%	b					
1.7.4 2 years									
Chan Weam Benedict Peng. 2009	16.2	3.4	29	17.5	3.8	29	1.4%	-1.30 [-3.16, 0.56]	+
Chusheng seng et al. 2013	19.2	3.4	40	19.3	2.5	40	3.0%	-0.10 [-1.36, 1.16]	
F. Zairi 2013	30.1	2.1	40	31.5	1.4	60	8.7%	-1.40 [-2.14, -0.66]	
Olevien - D 204 5							0.500	0.0017.0014.001	
	10	6.6	30	12	5.8	34	0.5%	-2.00 [-5.06, 1.06]	
John K. Houten 2011	0	0	35	0	0	32		Not estimable	
John K. Houten 2011	0 21.4	0 20.9	35 72	0 20.7	0 16.5	32 72	0.1%		
John K. Houten 2011 Kong et al. 2012	0 21.4	0	35 72	0 20.7 15.33	0	32		Not estimable	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013	0 21.4	0 20.9	35 72	0 20.7	0 16.5	32 72	0.1%	Not estimable 0.70 [-5.45, 6.85]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015	0 21.4 12.25	0 20.9 10.52	35 72 12	0 20.7 15.33	0 16.5 17.64	32 72 12	0.1% 0.0%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011	0 21.4 12.25 20.61 28.5	0 20.9 10.52 3.34 11.4	35 72 12 33 42	0 20.7 15.33 25.81 36.5	0 16.5 17.64 3.47 11.6	32 72 12 37	0.1% 0.0% 1.9% 0.2%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015	0 21.4 12.25 20.61 28.5 12.9	0 20.9 10.52 3.34 11.4 9.9	35 72 12 33 42 42	0 20.7 15.33 25.81 36.5 16.5	0 16.5 17.64 3.47 11.6 11.3	32 72 12 37 45 54	0.1% 0.0% 1.9% 0.2% 0.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011	0 21.4 12.25 20.61 28.5 12.9 15.7	0 20.9 10.52 3.34 11.4 9.9 8.9	35 72 12 33 42 42 15	0 20.7 15.33 25.81 36.5 16.5 17.1	0 16.5 17.64 3.47 11.6 11.3 9.5	32 72 12 37 45 54 15	0.1% 0.0% 1.9% 0.2% 0.3% 0.1%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013	0 21.4 12.25 20.61 28.5 12.9 15.7 11	0 20.9 10.52 3.34 11.4 9.9 8.9 9.4	35 72 12 33 42 42 15 50	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3	32 72 37 45 54 15 50	0.1% 0.0% 1.9% 0.2% 0.3% 0.1% 0.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shunwu, Fan 2010	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7	0 20.9 10.52 3.34 11.4 9.9 8.9 9.4 10.1	35 72 12 33 42 42 15 50 32	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4	32 72 12 37 45 54 15 50 30	0.1% 0.0% 1.9% 0.2% 0.3% 0.1% 0.3% 0.2%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shumwu, Fan 2010 Tang FuXing 2015	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5	0 20.9 10.52 3.34 11.4 9.9 8.9 9.4 10.1 7.8	35 72 12 33 42 42 15 50 32 28	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3	32 72 12 37 45 54 15 50 30 30	0.1% 0.0% 1.9% 0.2% 0.3% 0.1% 0.3% 0.2% 0.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Hong Li 2011	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8	0 20.9 10.52 3.34 11.4 9.9 8.9 9.4 10.1 7.8 1.5	35 72 12 33 42 42 15 50 32 28 41	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1	32 72 12 37 45 54 15 50 30 30 30 38	0.1% 0.0% 1.9% 0.2% 0.3% 0.1% 0.3% 0.2% 0.3% 15.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Socott et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Hong Li 2011	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13	0 20.9 10.52 3.34 11.4 9.9 8.9 9.4 10.1 7.8 1.5 4	35 72 12 33 42 42 15 50 32 28 41 172	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8 13	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5	32 72 12 37 45 54 15 50 30 30 38 11	0.1% 0.0% 1.9% 0.2% 0.3% 0.3% 0.2% 0.3% 15.3% 0.5%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-5.6, 0.56] 0.00 [-3.01, 3.01]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Hong Li 2011 Wang Hong Li 2011	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8	0 20.9 10.52 3.34 11.4 9.9 8.9 9.4 10.1 7.8 1.5	35 72 12 33 42 42 15 50 32 28 41	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1	32 72 12 37 45 54 15 50 30 30 30 38	0.1% 0.0% 1.9% 0.2% 0.3% 0.1% 0.3% 0.2% 0.3% 15.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Socott et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Hong Li 2011 Wang Jin 2011	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13	0 20.9 10.52 3.34 11.4 9.9 8.9 9.4 10.1 7.8 1.5 4	35 72 12 33 42 42 15 50 32 28 41 172	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8 13	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5	32 72 12 37 45 54 15 50 30 30 38 11	0.1% 0.0% 1.9% 0.2% 0.3% 0.3% 0.2% 0.3% 15.3% 0.5%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-5.6, 0.56] 0.00 [-3.01, 3.01]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shumwu, Fan 2010 Tang FuXing 2015 Wang Jian 2011 Yang Jin 2013 Yang Yang 2015	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13 14.26	0 20.9 10.52 3.34 11.4 9.9 8.9 9.4 10.1 7.8 1.5 4 3.3	35 72 12 33 42 42 15 50 32 28 41 172 43	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8 13 14.87	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5 2.53	32 72 12 37 45 54 15 50 30 30 30 38 11 104	0.1% 0.0% 1.9% 0.2% 0.3% 0.3% 0.2% 0.3% 15.3% 0.5% 3.9%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56] 0.00 [-3.01], 3.01] -0.61 [-1.71, 0.49] -0.40 [-2.85, 2.05]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Hong Li 2011 Wang Jian 2011 Yang Jin 2013 Yang Yang 2015 Yi-bing Li 2015	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13 14.26 11.6 35.1	0 20.9 10.52 3.34 11.4 9.9 9.4 10.1 7.8 1.5 4 3.3 6.3 3.6	35 72 12 33 42 42 15 50 32 28 41 172 43 50 95	0 20.7 15.33 25.81 36.5 17.1 15.6 27.2 22.3 8 13 14.87 12 37.6	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5 2.53 6.2 4.3	32 72 12 37 45 54 15 50 30 30 30 38 11 104 50 79	0.1% 0.0% 1.9% 0.2% 0.3% 0.3% 15.3% 0.5% 3.9% 0.8% 3.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56] 0.00 [-3.01, 3.01] -0.61 [-1.71, 0.49] -0.40 [-2.85, 2.05] -2.50 [-3.69, -1.31]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Socott et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Jian 2011 Yang Jin 2013 Yang Yang 2015 Yi-bing Li 2015 Zhang Wen Zhi 2013	0 21.4 12.25 20.61 28.5 12.9 15.7 21.5 8 13 14.26 11.6	0 20.9 10.52 3.34 11.4 9.9 9.4 10.1 7.8 1.5 4 3.3 6.3	35 72 12 33 42 42 15 50 32 28 41 172 43 50 95 82	0 20.7 15.33 25.81 36.5 17.1 15.6 27.2 22.3 8 13 14.87 12	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5 2.53 6.2	32 72 12 37 45 54 15 50 30 30 30 38 11 104 50 79 76	0.1% 0.0% 1.9% 0.2% 0.3% 0.3% 0.3% 15.3% 0.5% 3.9% 0.8% 3.3% 1.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56] 0.00 [-3.01, 3.01] -0.61 [-1.71, 0.49] -0.40 [-2.85, 2.05] -2.50 [-3.69, -1.31] -1.10 [-2.99, 0.79]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shumwu, Fan 2010 Tang FuXing 2015 Wang Jian 2011 Yang Un 2013 Yang Yang 2015 Yi-bing Li 2015 Zhang Wen Zhi 2013 Subtotal (195% C1) Heterogeneity: Chi <sup>2</sup> = 63.39, df = 18	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13 14.26 11.6 35.1 13.2 9 (P < 0.00	0 20.9 10.52 3.34 11.4 9.9 9.4 10.1 7.8 1.5 4 3.3 6.3 3.6 5.1	35 72 12 33 42 42 15 50 32 28 41 172 43 50 95 82 948	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8 13 14.87 12 37.6 14.3	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5 2.53 6.2 4.3	32 72 12 37 45 54 15 50 30 30 30 38 11 104 50 79	0.1% 0.0% 1.9% 0.2% 0.3% 0.3% 15.3% 0.5% 3.9% 0.8% 3.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56] 0.00 [-3.01, 3.01] -0.61 [-1.71, 0.49] -0.40 [-2.85, 2.05] -2.50 [-3.69, -1.31]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shumwu, Fan 2010 Tang FuXing 2015 Wang Jian 2011 Yang Jin 2013 Yang Yang 2015 Yi-bing Li 2015 Zhang Wen Zhi 2013 Subtotal (195% C1) Heterogeneity: Chi <sup>2</sup> = 63.39, df = 18	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13 14.26 11.6 35.1 13.2 9 (P < 0.00	0 20.9 10.52 3.34 11.4 9.9 9.4 10.1 7.8 1.5 4 3.3 6.3 3.6 5.1	35 72 12 33 42 42 15 50 32 28 41 172 43 50 95 82 948	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8 13 14.87 12 37.6 14.3	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5 2.53 6.2 4.3	32 72 12 37 45 54 15 50 30 30 30 38 11 104 50 79 76	0.1% 0.0% 1.9% 0.2% 0.3% 0.3% 0.3% 15.3% 0.5% 3.9% 0.8% 3.3% 1.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56] 0.00 [-3.01, 3.01] -0.61 [-1.71, 0.49] -0.40 [-2.85, 2.05] -2.50 [-3.69, -1.31] -1.10 [-2.99, 0.79]	
Giovanni B 2015 John K. Houten 2011 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Hong Li 2011 Wang Jian 2011 Yang Jian 2011 Yang Yang 2015 Yi-bing Li 2015 Zhang Wen Zhi 2013 Subtotal (95% CI) Heterogeneity: Chi <sup>2</sup> = 63.39, df = 18 Test for overall effect: Z = 5.88 (P <	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13 14.26 11.6 35.1 13.2 9 (P < 0.00	0 20.9 10.52 3.34 11.4 9.9 9.4 10.1 7.8 1.5 4 3.3 6.3 3.6 5.1	35 72 12 33 42 42 15 50 32 28 41 172 43 50 95 82 948 *= 72%	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8 13 14.87 12 37.6 14.3	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5 2.53 6.2 4.3	32 72 12 37 45 54 15 30 30 30 30 30 30 30 30 30 70 866	0.1% 0.0% 1.9% 0.2% 0.3% 0.2% 0.3% 15.3% 0.5% 3.9% 0.8% 3.3% 1.3% 42.2%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56] 0.00 [-3.01, 3.01] -0.61 [-1.71, 0.49] -2.50 [-3.69, -1.31] -1.10 [-2.99, 0.79] -1.01 [-1.34, -0.67]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Scott et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Jan 2011 Yang Jin 2013 Yang Yang 2015 Yi-bing Li 2015 Zhang Wen Zhi 2013 Subtotal (95% Cl) Heterogeneity: Chi <sup>2</sup> = 63.39, df = 18 Test for overall effect: Z = 5.88 (P < Total (95% Cl)	0 21.4 12.25 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13 14.26 11.6 35.1 13.2 8 (P < 0.00 0.00001)	0 20.9 10.52 3.34 11.4 9.9 9.4 10.1 7.8 1.5 4 3.3 6.3 3.6 5.1	35 72 12 33 42 42 15 50 22 28 41 172 43 50 95 82 948 *= 72%	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8 3 14.87 12 37.6 14.3	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5 2.53 6.2 4.3	32 72 12 37 45 54 15 30 30 30 30 30 30 30 30 30 70 866	0.1% 0.0% 1.9% 0.2% 0.3% 0.3% 0.3% 15.3% 0.5% 3.9% 0.8% 3.3% 1.3%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56] 0.00 [-3.01, 3.01] -0.61 [-1.71, 0.49] -0.40 [-2.85, 2.05] -2.50 [-3.69, -1.31] -1.10 [-2.99, 0.79]	
John K. Houten 2011 Kong et al. 2012 Kriangsak Saetia 2013 Li Yu 2015 Liang Bo Wei 2011 Luo Zhi Ping 2015 Owoicho et al. 2011 Socht et al. 2013 Shunwu, Fan 2010 Tang FuXing 2015 Wang Jian 2011 Yang Jin 2013 Yang Yang 2015 Yi-bing Li 2015 Zhang Wen Zhi 2013 Subtotal (95% CI) Heterogeneity: Chi <sup>™</sup> = 63.39, df = 18 Test for overall effect: Z = 5.88 (P <	0 21.4 12.55 20.61 28.5 12.9 15.7 11 24.7 21.5 8 13 14.26 35.1 13.2 9 (P < 0.00 0.00001)	0 20.9 10.52 3.34 11.4 9.9 9.4 10.1 7.8 1.5 4 3.3 6.3 3.6 5.1 00001); 1 <sup>2</sup>	35 72 12 33 42 42 15 50 22 28 41 172 43 50 95 82 948 *= 72%	0 20.7 15.33 25.81 36.5 16.5 17.1 15.6 27.2 22.3 8 3 14.87 12 37.6 14.3	0 16.5 17.64 3.47 11.6 11.3 9.5 10.3 8.4 8.3 1 5 2.53 6.2 4.3	32 72 12 37 45 54 15 30 30 30 30 30 30 30 30 30 70 866	0.1% 0.0% 1.9% 0.2% 0.3% 0.2% 0.3% 15.3% 0.5% 3.9% 0.8% 3.3% 1.3% 42.2%	Not estimable 0.70 [-5.45, 6.85] -3.08 [-14.70, 8.54] -5.20 [-6.80, -3.60] -8.00 [-12.83, -3.17] -3.60 [-7.85, 0.65] -1.40 [-7.99, 5.19] -4.60 [-8.47, -0.73] -2.50 [-7.11, 2.11] -0.80 [-4.94, 3.34] 0.00 [-0.56, 0.56] 0.00 [-3.01, 3.01] -0.61 [-1.71, 0.49] -2.50 [-3.69, -1.31] -1.10 [-2.99, 0.79] -1.01 [-1.34, -0.67]	

Figure 8: ODI scores comparison between MIS and open groups at different follow-up intervals.

data on mental component scores from four studies showed no statistically significant differences (Figure 10).

	MIS		Oper	1		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
1.8.1 6 months							
Chusheng seng et al. 2013	19	40	26	40	17.8%	0.49 [0.20, 1.20]	
Kong et al. 2012	43	72	38	72	19.9%	1.33 [0.69, 2.57]	
Li Yu 2015	16	33	20	37	12.7%	0.80 [0.31, 2.05]	
Subtotal (95% CI)		145		149	50.4%	0.90 [0.57, 1.42]	· · · · · · · · · · · · · · · · · · ·
Total events	78		84				
Heterogeneity: Chi <sup>2</sup> = 3.18, df = 2 (P	= 0.20); l <sup>a</sup>	= 37%					
Test for overall effect: Z = 0.46 (P =	0.65)						
1.8.2 2 years							
Chan Weam Benedict Peng. 2009	24	29	26	29	5.8%	0.55 [0.12, 2.57]	
Chusheng seng et al. 2013	35	40	36	40	5.9%	0.78 [0.19, 3.14]	· · · · ·
Jason S. Cheng 2013	46	50	25	25	3.9%	0.20 [0.01, 3.92]	
Kong et al. 2012	70	72	71	72	2.6%	0.49 [0.04, 5.56]	
Kriangsak Saetia 2013	11	12	11	12	1.2%	1.00 [0.06, 18.08]	
Li Yu 2015	30	33	31	37	3.5%	1.94 [0.44, 8.45]	
Shu Dong Ping 2016	32	35	29	35	3.2%	2.21 [0.51, 9.64]	
Wang Jian 2011	166	172	194	199	8.2%	0.71 [0.21, 2.38]	· · ·
Yan XiongWei 2016	48	51	44	46	3.5%	0.73 [0.12, 4.56]	· · · · · · · · · · · · · · · · · · ·
Yang Yang 2015	44	50	45	50	7.0%	0.81 [0.23, 2.87]	
Zhang Wen Zhi 2013	78	82	73	76	4.8%	0.80 [0.17, 3.70]	
Subtotal (95% CI)		626		621	49.6%	0.86 [0.54, 1.38]	◆
Total events	584		585				
Heterogeneity: Chi <sup>2</sup> = 4.33, df = 10 (	P = 0.93);	l <sup>2</sup> = 0%					
Test for overall effect: Z = 0.61 (P =	0.54)						
Total (95% CI)		771		770	100.0%	0.88 [0.64, 1.22]	+
Total events	662		669				
Heterogeneity: Chi <sup>2</sup> = 7.52, df = 13 (	P = 0.87);	l² = 0%					
Test for overall effect: Z = 0.76 (P =							0.01 0.1 1 10 1
Test for subaroup differences: Chi² =		1 (P =	0.91). I <sup>2</sup> :	= 0%			Favours [experimental] Favours [control]

Figure 9: Fusion rate comparison between MIS and open groups.

		MIS			Open			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Tota	Weight	IV, Fixed, 95% C	IV, Fixed, 95% CI
1.10.2 mental component sco	ores								
Chusheng seng et al. 2013	51.1	14.1	40	50.5	10.9	40	15.6%	0.60 [-4.92, 6.12]	+
Javier Rodrı´guez-Vela 2013	62.62	19.66	21	55.464	20.8	20	3.1%	7.16 [-5.25, 19.56]	
Owoicho Adogwa 2012	4.7	10.47	14	7.18	9.17	7	6.2%	-2.48 [-11.21, 6.25]	
Scott et al. 2013	54.4	10.8	50	52	10.1	50	28.3%	2.40 [-1.70, 6.50]	<b>•</b>
Subtotal (95% CI)			125			117	53.2%	1.58 [-1.41, 4.57]	•
Heterogeneity: Chi <sup>2</sup> = 1.88, df =	= 3 (P = 0	.60); I <sup>2</sup> :	= 0%						
Test for overall effect: Z = 1.03	(P = 0.30	))							
1.10.3 physical component s	cores								
Chusheng seng et al. 2013	47.4	11.8	40	46.1	12.6	40	16.6%	1.30 [-4.05, 6.65]	+
Javier Rodrı´guez-Vela 2013	57.199	20.8	21	50.599	24.7	20	2.4%	6.60 [-7.41, 20.61]	
Owoicho Adogwa 2012	14.78	11.08	14	5.13	11.57	7	4.4%	9.65 [-0.70, 20.00]	
Scott et al. 2013	44.3	11.2	50	41.3	11.8	50	23.4%	3.00 [-1.51, 7.51]	
Subtotal (95% CI)			125			117	46.8%	3.21 [0.03, 6.40]	●.
Heterogeneity: Chi <sup>2</sup> = 2.21, df =	= 3 (P = 0	.53); I <sup>2</sup> :	= 0%						
Test for overall effect: Z = 1.98	(P = 0.05	5)							
Total (95% CI)			250			234	100.0%	2.34 [0.16, 4.52]	•
Heterogeneity: Chi <sup>2</sup> = 4.63, df =	= 7 (P = 0	.70); 12:	= 0%						-100 -50 0 50 100
Test for overall effect: Z = 2.11	(P = 0.04	4)							
Test for subaroup differences:	Chi² = 0.5	54. df =	1 (P = 1	0.46), I <sup>2</sup> =	0%				Favours (experimental) Favours (control)

Figure 10: Short-form 36 physical and mental component scores.

#### 4.11 Neurogenic Symptom Scores

At the 6-month follow-up, neurogenic symptom scores were reported in three studies. One of these showed statistically significant differences, with a mean difference (MD) of 1.87 (95% CI: 0.67 to 3.07). There was no evidence of heterogeneity ( $I^2 = 0\%$ , P = 0.77; Figure 11). At

the 2-year follow-up, although no individual study reported significant differences, pooled data indicated that the open group had lower neurogenic symptom scores than the MIS group, with a WMD of -1.44 (95% CI: 0.50 to 2.38, P = 0.003). Again, there was no evidence of heterogeneity (I<sup>2</sup> = 0%, P = 0.71; Figure 11).

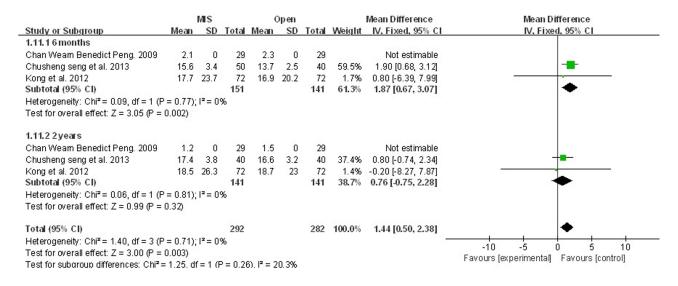


Figure 11: Neurogenic symptom scores at 6-month and 2-year follow-ups.

## 4.12 Biochemical Markers of Inflammation and Muscle Damage

### 4.12.1 C-reactive Protein (CRP)

CRP levels were measured in four studies at 24 hours post-operation. The minimally invasive surgery (MIS) group exhibited significantly lower CRP levels than the open group, with a weighted mean difference (WMD) of -17.20 ng/L (95% CI: -27.05 to -7.35), although significant heterogeneity was present (I<sup>2</sup> = 89%, random effects). At 7 days post-operation, CRP levels were reported in two studies, showing no significant differences between the groups (WMD = -3.51 ng/L; 95% CI: -16.17 to 9.16), with very high heterogeneity (I<sup>2</sup> = 98%). Overall, CRP levels in the MIS group were 12.45 ng/L lower than those in the open group (WMD = -12.45; 95% CI: -21.43 to -3.47), also displaying substantial heterogeneity (I<sup>2</sup> = 97%, Figure 12).

### 4.12.2 CK-MM

CK-MM levels recorded 24 hours after surgery in three studies showed that the MIS group had significantly lower levels than the open group by 178.62 IU/L (WMD = -178.62; 95% CI: -269.66 to -87.57), with evident heterogeneity (I<sup>2</sup> = 88%). At 7 days post-operation, CK-MM levels were lower in the MIS group by 16.60 IU/L (WMD = -16.60; 95% CI: -33.47 to 0.27), showing moderate heterogeneity (I<sup>2</sup> = 55%). Cumulatively, CK-MM levels in the MIS group were 87.64 IU/L lower than in the open group (WMD = -87.64; 95% CI: -136.10 to -39.17), with high heterogeneity (I<sup>2</sup> = 94%, Figure 13).

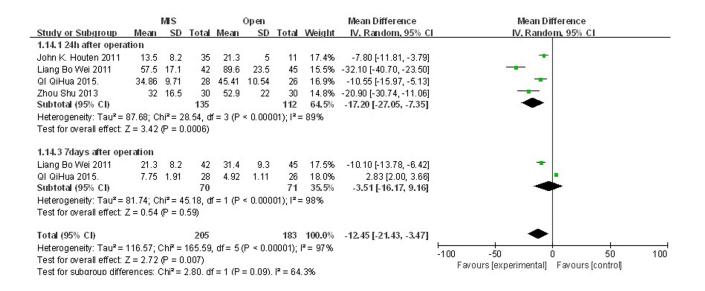


Figure 12: C-reactive protein (CRP) levels comparison between MIS and open groups.

MIS Open							Mean Difference	Mean Difference
Mean	SD	Tota	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
302.3	134.9	42	587.7	223.7	45	12.8%	-285.40 [-362.45, -208.35]	
202.48	53.21	28	312.84	73.62	26	17.3%	-110.36 [-144.85, -75.87]	
280.5	80.9	30	437.2	137.5	30	15.0%	-156.70 [-213.79, -99.61]	
		100			101	45.0%	-178.62 [-269.66, -87.57]	
5610.85;	Chi <sup>2</sup> = 1	6.78, d	lf= 2 (P =	= 0.000:	2); I <sup>2</sup> =	88%		
z = 3.85 (	(P = 0.0	001)						
129.1	51.4	42	138.4	55.8	45	18.2%	-9.30 [-31.83, 13.23]	-
93.86	26.32	28	125.35	35.83	26	18.5%	-31.49 [-48.36, -14.62]	+
91.9	36.9	32	97.9	42.5	30	18.3%	-6.00 [-25.87, 13.87]	
		102			101	55.0%	-16.60 [-33.47, 0.27]	•
21.81; C	h <b>r</b> = 4.	43, df =	2 (P = 0	), 11); P	= 55%			
2 = 1.93 (	(P = 0.0	5)						
		202			202	100.0%	-87.64 [-136.10, -39.17]	•
3234.39;	Chi <sup>2</sup> = 8	9.71, d	lf= 5 (P -	< 0.000	01); I <sup>z</sup> =	94%		
2 = 3.54 (	(P = 0.0	004)	3		1			-200 -100 0 100 200
	•		= 1 (P =	0.0006	$ ^{2} = 9$	1.5%		MIS Open
	Mean 302.3 202.48 280.5 5610.85; 2.3.85 129.1 93.86 91.9 (21.81; C (21.81; C (21.81; C) (21.81; C) (234.39; (2.34.39; C) (2.34.39; C) (2.34.39; C) (2.35, C) (	Mean         SD $302.3$ $134.9$ $202.48$ $53.21$ $280.5$ $80.9$ $5610.86$ ; $Chi^2 = 1$ $2 = 3.85$ (P = 0.0 $129.1$ $51.4$ $93.86$ $26.32$ $91.9$ $36.9$ $21.81$ ; $ChF = 4$ . $2 = 1.93$ (P = 0.0 $3234.39$ ; $Chi^2 = 8$ $2 = 3.54$ (P = 0.0	Mean         SD         Total $302.3$ $134.9$ $42$ $202.48$ $53.21$ $28$ $280.5$ $80.9$ $30$ $100$ $5610.85$ ; Chi² = $16.78$ , c $5610.85$ ; Chi² = $16.78$ , c $100$ $5610.85$ ; Chi² = $16.78$ , c $100$ $129.1$ $51.4$ $42$ $93.86$ $26.32$ $28$ $91.9$ $36.9$ $32$ $102$ $102$ $102$ $21.81$ ; Chř = $4.43$ , df = $= 1.93$ (P = $0.05$ ) $202$ $8234.39$ ; Chi² = $89.71$ , c $= 3.54$ (P = $0.0004$ )	Mean         SD         Total         Mean $302.3$ $134.9$ $42$ $587.7$ $202.48$ $53.21$ $28$ $312.84$ $280.5$ $80.9$ $30$ $437.2$ $100$ $5610.85;$ Chi² = 16.78, df = 2 (P = 2) $129.1$ $51.4$ $42$ $138.4$ $93.86$ $26.32$ $28$ $125.35$ $91.9$ $36.9$ $32$ $97.9$ $102$ $121.81;$ Chr² = 4.43,         df = 2 (P = 0) $21.81;$ Chr² = $89.71,$ df = 5 (P = 0) $3234.39;$ Chi² = $89.71,$ df = 5 (P = 0)	Mean         SD         Total         Mean         SD $302.3$ $134.9$ $42$ $587.7$ $223.7$ $202.48$ $53.21$ $28$ $312.84$ $73.62$ $280.5$ $80.9$ $30$ $437.2$ $137.5$ $100$ $5610.85$ ; Chi² = $16.78$ , df = $2$ (P = $0.0001$ ) $129.1$ $51.4$ $42$ $138.4$ $55.8$ $93.86$ $26.32$ $28$ $125.35$ $35.83$ $91.9$ $36.9$ $32$ $97.9$ $42.5$ $102$ $121.81$ ; Ch² = $4.43$ , df = $2$ (P = $0.11$ ); l² $12.93$ (P = $0.05$ ) $202$ $8234.39$ ; Chi² = $89.71$ , df = $5$ (P < $0.0001$ ) $202$ $83.43$ (P = $0.0004$ ) $132.47$ $133.54$ (P = $0.0004$ ) $132.47$	Mean         SD         Total         Mean         SD         Total $302.3$ $134.9$ $42$ $587.7$ $223.7$ $45$ $202.48$ $53.21$ $28$ $312.84$ $73.62$ $26$ $280.5$ $80.9$ $30$ $437.2$ $137.5$ $30$ $100$ $101$ $101$ $101$ $101$ $5610.85$ ; Chi² = 16.78, df = 2 (P = 0.0002); l² = 12 $283.5$ $26.2$ $283.5$ $45.9$ $38.5$ $P = 0.0001$ ) $101$ $101$ $101$ $101$ $129.1$ $51.4$ $42$ $138.4$ $55.8$ $45$ $93.86$ $26.32$ $28$ $125.35$ $35.83$ $26$ $91.9$ $36.9$ $32$ $97.9$ $42.5$ $30$ $102$ $101$ $101$ $101$ $101$ $101$ $121.81$ ; ChF = 4.43, df = 2 (P = 0.11); l² = 55\% $= 1.93$ (P = 0.05) $202$ $202$ $202$ $2324.39$ ; Chi² = 89.71, df = 5 (P < 0.00001); l² = $13.54$ (P	Mean         SD         Total         Mean         SD         Total         Weight           302.3         134.9         42         587.7         223.7         45         12.8%           202.48         53.21         28         312.84         73.62         26         17.3%           280.5         80.9         30         437.2         137.5         30         15.0%           100         101         45.0%         100         101         45.0%           5610.85; Chi² = 16.78, df = 2 (P = 0.0002); I² = 88%         18.2%         93.86         26.32         28         125.35         35.83         26         18.5%           91.9         36.9         32         97.9         42.5         30         18.3%           91.9         36.9         32         97.9         42.5         30         18.3%           91.9         36.9         32         97.9         42.5         30         18.3%           91.9         36.9         32         97.9         42.5         30         18.3%           102         101         55.0%         19.1%         19.55%         19.1%         19.55%           1.93 (P = 0.05)         202         <	MeanSDTotalMeanSDTotalWeightIV. Random, 95% CI $302.3$ $134.9$ $42$ $587.7$ $223.7$ $45$ $12.8\%$ $-285.40$ $[-362.45, -208.35]$ $202.48$ $53.21$ $28$ $312.84$ $73.62$ $26$ $17.3\%$ $-110.36$ $[-144.85, -75.87]$ $280.5$ $80.9$ $30$ $437.2$ $137.5$ $30$ $15.0\%$ $-156.70$ $[-213.79, -99.61]$ $100$ $101$ $45.0\%$ $-178.62$ $[-269.66, -87.57]$ $5610.85$ $Chi^2 = 16.78$ , $df = 2$ (P = $0.0002$ ); I <sup>2</sup> = $88\%$ $-9.30$ $[-31.83, 13.23]$ $93.86$ $26.32$ $28$ $125.35$ $35.83$ $26$ $18.5\%$ $-31.49$ $91.9$ $36.9$ $32$ $97.9$ $42.5$ $30$ $18.3\%$ $-6.00$ $102$ $101$ $55.0\%$ $-16.60$ $[-33.47, 0.27]$ $21.81$ ; $ChP = 4.43$ , $df = 2$ (P = $0.11$ ); I <sup>2</sup> = $55\%$ $= 1.93$ (P = $0.05$ ) $-87.64$ $[-136.10, -39.17]$ $3234.39$ ; $Chi^2 = 89.71$ , $df = 5$ (P < $0.00001$ ); I <sup>2</sup> = $94\%$ $= 3.54$ (P = $0.0004$ ) $= 3.54$ (P = $0.0004$ )

Figure 13: Creatine kinase-MM (CK-MM) levels comparison between MIS and open groups.

#### 4.12.3 CPK Levels

CPK levels recorded 24 hours post-operation were available in three studies. The minimally invasive surgery (MIS) group had significantly lower CPK levels compared to the open group, with a weighted mean difference (WMD) of -84.17 IU/L (95% CI: -93.40 to -74.95, P < 0.00001). There was significant heterogeneity among the studies (I<sup>2</sup> = 91%). At 7 days post-operation, data from two studies showed no statistically significant differences between the groups (WMD = -0.72, 95% CI: -4.95 to 3.51), with low heterogeneity (I<sup>2</sup> = 43%). Overall, the MIS group had lower CPK levels by 15.24 IU/L compared to the open group (WMD = -15.24, 95% CI: -19.09 to -11.40), with substantial heterogeneity (I<sup>2</sup> = 99%, Figure 14).

	MIS		Open				Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% CI
1.16.1 24h CPK									
Li Yu 2015	486.32	21.09	33	573.55	18.36	37	17.0%	-87.23 [-96.55, -77.91]	
Owoicho Adogwa 2012	739	1,002	14	387	242	7	0.0%	352.00 [-202.64, 906.64]	· · · · · · · · · · · · · · · · · · ·
Wang Hong Li 2011	547.6	175.7	41	484.1	120.8	38	0.3%	63.50 [-2.59, 129.59]	· · · · · · · · · · · · · · · · · · ·
Subtotal (95% CI)			88			82	17.4%	-84.17 [-93.40, -74.95]	•
Heterogeneity: Chi <sup>2</sup> = 21.9	97, df = 2	(P < 0.	0001);1	<sup>2</sup> = 91%					
Test for overall effect: Z =	17.89 (P	< 0.00	001)						
1.16.2 7days CPK									
Li Yu 2015	86.72	11.59	33	90.14	13.24	37	43.7%	-3.42 [-9.24, 2.40]	-
Wang Hong Li 2011	49.7	16.2	41	47.4	11.5	38	38.9%	2.30 [-3.86, 8.46]	· · · · · · · · · · · · · · · · · · ·
Subtotal (95% CI)			74			75	82.6%	-0.72 [-4.95, 3.51]	★
Heterogeneity: Chi2 = 1.75	5, df = 1 (	(P = 0.1)	9); I <sup>2</sup> =	43%					
Test for overall effect: Z =	0.34 (P :	= 0.74)							
Total (95% CI)			162			157	100.0%	-15.23 [-19.07, -11.38]	▲
Heterogeneity: Chi <sup>2</sup> = 283	.56. df =	4 (P < (	0.00001	); <b> </b> <sup>2</sup> = 99	%				
Test for overall effect: $Z = 7.76$ (P < 0.00001)						-100 -50 0 50 100			
Test for subaroup differences: $Chi^2 = 259.84$ , df = 1 (P < 0.00001), $I^2 = 99.6\%$						Favours [experimental] Favours [control]			

Figure 14: Creatine phosphokinase (CPK) levels comparison between MIS and open groups.

#### 4.12.4 Complication Rates

Complication rates were reported in 13 studies. There were no statistically significant differences in complication rates between the MIS and open groups ( $I^2 = 12\%$ , Figure 15).

	MIS		Oper	1		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Alan T.Villavicencio 2011	20	63	24	76	20.1%	1.01 [0.49, 2.07]	
Chu Ya Wei 2014	1	15	2	36	1.5%	1.21 [0.10, 14.50]	· · · · · · · · · · · · · · · · · · ·
Darryl Lau 2013	9	78	14	49	20.6%	0.33 [0.13, 0.83]	
Dhall SS 2008	3	54	2	53	2.6%	1.50 [0.24, 9.36]	
F. Zairi 2013	1	40	5	60	5.3%	0.28 [0.03, 2.51]	
Giovanni B 2015	1	30	2	34	2.5%	0.55 [0.05, 6.41]	· · · · · · · · · · · · · · · · · · ·
Hwee Weng Dennis Hey 2015	8	25	2	25	1.8%	5.41 [1.02, 28.79]	
Shunwu, Fan 2010	6	32	5	30	5.7%	1.15 [0.31, 4.27]	
Wang Jian 2011	21	172	25	199	27.5%	0.97 [0.52, 1.80]	20 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Yan XiongWei 2016	0	51	2	46	3.5%	0.17 [0.01, 3.70]	· · · · ·
Yang Jin 2013	3	43	4	104	2.9%	1.88 [0.40, 8.76]	
Yang Yang 2015	5	50	4	50	4.9%	1.28 [0.32, 5.07]	
You Lv 2017	2	50	1	56	1.2%	2.29 [0.20, 26.07]	
Total (95% CI)		703		818	100.0%	0.94 [0.68, 1.30]	+
Total events	80		92				
Heterogeneity: Chi <sup>z</sup> = 13.61, df = 12 (P = 0.33); l <sup>z</sup> = 12%							
Test for overall effect: Z = 0.39 (	° = 0.70)						0.01 0.1 1 10 100 MIs-TLIF Open-TLIF

Figure 15: Comparison of complication rates between MIS and open groups.

## 5 Discussion

#### 5.1 Advantages and Limitations of TLIF and MIS-TLIF

TLIF, an evolution of posterior lumbar interbody fusion (PLIF), was first introduced in 1998<sup>[15]</sup>. It offers several advantages over PLIF, including reduced epidural synechiae and decreased scar formation. However, TLIF has limitations in contralateral decompression and incomplete disc

removal<sup>[16]</sup>. On the other hand, PLIF may result in abnormal physiological motion of the fused lumbar segments, increased stress on adjacent segments, and accelerated degeneration<sup>[17]</sup>.

With advancements in spine surgery, minimally invasive TLIF (MIS-TLIF) has emerged as a popular alternative. MIS-TLIF is associated with reduced intraoperative blood loss, faster recovery, and improved postoperative function<sup>[18]</sup>. However, it also has limitations, such as restricted working space, potentially leading to longer operative times and a steeper learning curve<sup>[19]</sup>. According to Lee et al.<sup>[20]</sup>, surgeons must perform 44 MIS-TLIF procedures to reach proficiency. Additionally, MIS-TLIF has been reported to increase surgical risks by up to 31.37%<sup>[21]</sup>, including cage misplacement, screw misalignment, and nerve root injury. A contentious issue surrounding MIS-TLIF is the increased intraoperative fluoroscopy exposures, challenging surgeons to choose between minimally invasive and open techniques<sup>[22]</sup>.

#### 5.2 Surgical Exposure and Long-Term Outcomes

One of the major drawbacks of MIS-TLIF is reduced surgical exposure and visualization, which can lead to insufficient neural decompression. This inadequate decompression may reduce the long-term efficacy of the surgery<sup>[5]</sup>. Although high-quality evidence supports the short-term benefits of MIS-TLIF, its long-term outcomes remain uncertain<sup>[18]</sup>. Our meta-analysis sought to compare the long-term clinical outcomes of MIS-TLIF and open-TLIF in treating single-level degenerative lumbar diseases, with follow-up periods exceeding two years.

Previous meta-analyses by Sun et al.<sup>[23]</sup>, Tian et al.<sup>[24]</sup>, and Nickalus et al.<sup>[25]</sup> found that MIS-TLIF resulted in less blood loss and shorter hospital stays compared to open-TLIF. However, these studies had limitations, including a lack of focus on VAS scores for leg pain and varying methodologies, potentially introducing bias. Additionally, these meta-analyses were restricted to English-language publications, potentially overlooking important data and contributing to publication bias<sup>[14,26]</sup>.

#### 5.3 Clinical Effectiveness of MIS-TLIF

Our meta-analysis confirmed that MIS-TLIF is associated with significantly lower blood loss and shorter hospital stays, with no significant difference in surgery time compared to open-TLIF. These findings align with previous studies<sup>[24]</sup>. Patients undergoing MIS-TLIF also showed less postoperative drainage volume. Regarding pain outcomes, MIS-TLIF led to better VAS back pain scores at follow-ups of  $\leq 6$  months, 1 year, and  $\geq 2$  years. However, the advantages for VAS leg pain were limited to the early postoperative period ( $\leq 6$  months). No significant differences in VAS leg pain were observed at the 1-year and 2-year follow-ups.

#### 5.4 Functional Outcomes and ODI Improvements

Our meta-analysis revealed superior early (1 month, 6 months) and mid-term (1 year, ⊡2 years) ODI score improvements in the MIS-TLIF group. However, the conclusions should be interpreted with caution. Although Sun et al.<sup>[23]</sup> found slight ODI improvement at 1-year follow-up,

Nickalus R et al.<sup>[25]</sup> reported no significant differences. Further high-quality studies are necessary to corroborate these findings.

## 5.5 Intraoperative Radiological Exposure

MIS-TLIF procedures are associated with longer intraoperative radiological exposure. Chang Hyeun Kim et al.<sup>[29]</sup> demonstrated that MIS-TLIF patients were exposed to 2.4 times more radiation than open-TLIF patients, with higher lifetime risks of cancer and hereditary disorders. However, the use of navigation-assisted fluoroscopy has shown potential for reducing intraoper-ative radiation exposure in minimally invasive spine surgeries<sup>[30]</sup>.

## 5.6 Learning Curve and Technical Challenges

The steep learning curve of MIS-TLIF can significantly affect surgery time and radiation exposure. With advancements in technology and surgeon proficiency, it is anticipated that intraoperative radiological exposure time will decrease<sup>[20]</sup>. Comparative studies have shown that radiation doses vary depending on surgical technique and individual anatomy<sup>[31,32]</sup>.

## 5.7 Additional Clinical Outcomes and Fusion Rates

Our meta-analysis found no significant differences in SF-36 physical and mental component scores, nor in NASS scores for neurogenic symptoms, between MIS-TLIF and open-TLIF groups. Furthermore, fusion rates were comparable between the two procedures, consistent with prior research<sup>[34]</sup>. The complication rates were also similar between the two techniques<sup>[35]</sup>.

## 5.8 Biochemical Markers of Inflammation and Muscle Damage

CRP and CK-MM levels, commonly used markers of inflammation and muscle damage, were lower in the MIS-TLIF group post-operation. Lower CRP levels in the early postoperative period suggest reduced inflammatory response following MIS-TLIF, although there were no significant differences at 7 days post-operation. Similarly, CK-MM and CPK levels were significantly lower in the MIS-TLIF group 24 hours post-operation, indicating less muscle damage compared to open-TLIF<sup>[36,37,38]</sup>. These findings suggest that MIS-TLIF is associated with less iatrogenic muscle injury than open-TLIF.

## 5.9 Limitations

There are several limitations to our study. Firstly, there was a scarcity of high-quality randomized controlled trials (RCTs), which are crucial for evaluating surgical treatments. Consequently, we had to include retrospective and prospective studies, which are susceptible to selection bias. Many of these studies had methodological defects, leading to significant heterogeneity when continuous outcomes were pooled. Secondly, we did not analyze complications by specific types because the nature of complications varied across studies; instead, we only analyzed the overall complication

rate. Thirdly, the data we collected were not discharge values, which would have provided greater confidence in our findings. Despite these limitations, our systematic review still offers valuable insights for clinicians.

	72 J		Study	0.0	Methodological Quality				
Studies Chan Wearn Benedict Peng	Etiology Spondylolisthesis	Participants: Group 1: MIS TLIF Group 2: Open TLIF	Design	Outcome Collection	Assessment of Included Studies				
2009[39]	+ DDD	Group 1: 29 participants;mean age 54.1 year (26.4 −7.3.6 years), female:male 24:5 follow-up 22 years Group 2: 29 participants; mean age 54.1 year (26.−7.3.6 years) follow-up 22 years, female:male 24:5 Group 1: 15 participants; mean age 50.8 year (SD age 7.9 years) female:male ratio of 8.7 follow-up 22 years	PCS	1.2.3.4.5.6.7.9	S:3+C:2+O:3=8				
Owoicho Adogwa 2011[40]	Degenerative spondylolithesis	Group2: 15 participants mean age 49.7 year (SD age 11.4 years) female:male ratio of 10:5 follow-up ≥2 years	RCS	2.3.5.6.	S:4+C:1+O:3=8				
	Spondylolisthesis+ spinal stenosis+ DDD	Group 1: 33 participants, mean age 51.67 ± 12.19, female:male 23:10 Follow-up for2 years ;follow-up rate unclear Group 2: 33 participants, mean age 49.85 ± 10.72, female:male 21:12, follow-up for 2 years, follow-up rate unclear	PCS	2.3.4.5.	S:4+C:2+O:2=8				
Kong Hwee Lee 2012[42]	Spondylolisthesis+ recurrent prolapsed disc+ spinal stenosis+ degenerated collapsed disc	Group 1 :72 participants, age 52.2 ± 13.8, femal:male 52:20, follow-up 2 years ; follow-up rate 95.8% Group 2:72 participants, age 56.6 ± 14.6, femal:male 50:22, follow-up 2 years, follow-up rate 91.7%	PCS	1.2.3.4.5.6.7.9.	S:4+C:2+O:3=9				
	Spondylolisthesis	Group 1: 50 participants, age 53.5 $\pm$ 12.5 years, mean age 53.5 years (SD age 12.5), female:male 34:16, follow-up $\geq$ 2 year Group 2: 50 participants, age 52.6 $\pm$ 11.6 years, female:male 32:18, follow-up $\geq$ 2 year	PCS	5.6.8.	S:3+C:2+O:3=8				
Kern Singh 2014[44]	Spondylolisthesis+ Spinal stenosis+	Group 1: 33 participantsAge 51.67±11.12Femalemale 10:23Follow-up ≥2 years Group 2: 33 participantsAge 59.85±10.72Femalemale 12:21Follow-up ≥2 years	RCS	2.3.4	S:3+C:2+O:3=8				
	DDD Spondylolisthesis	Group 1: 57 participants, Mean age 61.1, female:male 40:17, follow-up ≥1 years	RCS	2.3.4.6	S:4+C:2+O:2=8				
Seng 2013[46]	Spondylolisthesis+	Group 2: 11 participants, mean age 56.7, female:male 7.4, follow-up ≥1 years Group 1: 40 participants, age 56.6 ± 1.63, female:male 33:7, follow-up ≥5 years	RCS	1.2.3.4.5.7.8.9	S:4+C:2+O:2=8				
Alan T.Villavicencio	DDD Spondylolisthesis + DDD+	Group 2: 40 participants, age 56.8 ± 1.67, female:male 33:7, follow-up ≥5 years Group1:76participants, age:50.5(19-91), female:male:31:45, follow-up:37.5(26-52)	RCS	2.3.4.14	S-4+C-2+O-2=8				
2010[47]	Stenosis	Group2:63participants;age: 58.9(30-86); female:male 25:38;follow-up:37.5(26-52) Group1:21participants;age:53.P:0.98;female:male:NA;follow-up:24(12-47),							
	Spondylolisthesis+ DDD Spondylolisthesis+	Group1:21participants.age:531:0:36, Grande:male:NA, follow-up:34(12-86) Group1:40participants.age:53.P.0.98, female:male:NA, follow-up:34(12-86) Group1:40participants.age:49:.P.0.723,female:male:20:20;follow-up:24(12-86)	RCS	2.3.14	S:4+C:2+O:2=8				
F. Zain 2015[49]	DDD Spondylolisthesis+	Group2: Oparticipants, age: 48. P.0.723, female:male:3547, follow-up:20(24-48) Group1: 30participants, age: 46(28-56); female:male:1312; follow-up:23(12-38),	RCS	2.3.14	S:3+C:2+O:3=8				
Giovanni B 2015[50]	DDD	Group2:34participants, age:51(32-58),female:male:20:14, follow-up:25(12-40)2	RCS	2.3.4.5.6.14	S:4+C:2+O:2=8				
2015[51]	NA	Group1:25participants;age44.4(19-69);female:male:12:13;follow-up:26.9 Group2:25participants, age:43.6(20-69),female:male:12:13,follow-up:29.3	PCS	2.3.4.14	S:3+C:2+O:2=7				
2013[52]	DDD	Group1:21participants, age:41.8±8.7;female:male:7:14, follow-up:>3 years Group2:20participants;age43.15±7.3;female:male:7:13;follow-up:>3 years	PCS	8	S:3+C:2+O:2=7				
Jian Wang 2010[53]	Degenerative spondylolisthes+ Isthmic spondylolisthes	Group1:42participants;age47.9±8.5;female:male:29:13;follow-up:26.3(13-35) Group2:43participants, age:53.2±10.6;female:male:27:13, follow-up:26.3(13-35)	PCS	2.3.4.5.6.10.14	S:4+C:2+O:2=8				
	Spondylolisthesis	Group1:12participants;age63.1±6.84;female:male:11:1;follow-up:28(24-38) Group2:12participants;age:67.4±10.35;female:male:6:6, follow-up:28(24-38)	RCS	2.3.4.6.7.	S:4+C:2+O:2=8				
Owoicho 2012[55]	Spondylolisthesis+ DDD	Group1:14participants;age48.14±13.21;female:male:10:4;follow-up:>2years Group2:7participants;age:47.28±9.86;female:male:4:3, follow-up:>2years	PCS	4.8	S:4+C:2+O:2=8				
	Spondylolisthesis+ DDD+	Group1:32participants;age51.4±7.2;femate:mate:tai14:18;follow-up;2years Group1:32participants;age51.4±7.2;femate:mate:16:14,16!low-up;2years	PCS	2.3.4.5.10.12.14	S:4+C:1+O:3=8				
	Stenosis Single-level LDH+ Spinal stenosis+	Goup1:41participants;age51.4±13.3;female:male:17:24;follow-up:32.7(24-47)	RCT	1.2.3.10.13	S:4+C:1+O:3=8				
	Spondylolisthesis Spinal stenosis +	Group2:38participants;age:57.3±12.1;female:male:15:23;follow-up:32.7(24-47) Goup1:50participants;age58.0±13.4;female:male:32:18;follow-up:2years							
	Spondylolisthesis + Disc herniation with segmental instability Lumbar	Group2:50participants;age:56.1±11.0;female:male:27:23;follow-up:2years	RCT	1.2.3.5.6.7.14	S:4+C:2+O:3=9				
Yi-bing Li 2016[59]	Instability+Lumbar stenosis+ Lumbar spondylolysis	Goop1:95participants;age:56.0±7.8;female:male:46:43;follow-up:51.8±6.8 Group2:79participants;age:59±5.5;female:male:47:45;follow-up:54.8±5.7 Goop1:15participants;	PCS	3.6	S:3+C:2+O:3=8				
Chu Ya Wei 2014[60]	DDD	Group2:36participants; Mean age in all cases: 53 (40-76) Female: Male in all cases: 17:34	RCS	2.3.6.10.14	S:3+C:2+O:3=8				
Darryl Lau2013[61]	Spondylolisthesis+ Degenerative disc disease (DDD).	Group1:26participants; Group2:19participants; Mean age: Group1: 490:5134. Group2: 57.4±12.6 FenalcMale: Group1:14:12;Group2:11:8	RCS	14	S:3+C:2+O:3=8				
	Lumbar degenerative disease	Goup1:33participants;age51.83±4.16;female:male:15:18;follow-up:23.57±3.05 Group2:37participants;age:52.42±3.76;female:male:16:21;follow-up:24.67±3.48	PCS	2.3.4.6.7.10.13	S:4+C:2+O:2=8				
Liang Bo Wei 2011[63]	Degenerative lumbar instability	Goup1:42participants;age49.8 (41-62) ;female:male:19:23;follow-up:32 (27-52) Group2:45participants;age:51.3 (38-65) ;female:male:19:26;follow-up:33 (26-51)	RCS	2.3.5.6.10.11	S:4+C:2+O:3=9				
Luo Zhi Ping 2015[64]	LDH with instability; Lumbar stenosis+ Lumbar spondylolysis;	Goup1:42participants;age64.4±4.9;fcmalc:male:19:23;follow-up:26±7 Group2:54participants;age:66.5±7.6;fcmalc:male:22:32;follow-up:27±8	RCT	2.3.6.10.11	S:4+C:2+O:3=9				
QI QI Hua 2015[65]	Spondylolisthesis+ DDD+	Goup1:28participants;age44.1 (35-55) ;female:male:12:16;follow-up:>1year Group2:26participants;age43.5 (39-60) ;female:male:11:15;follow-up:>1year	RCS	2.3.5.6.10.11.12	S:4+C:2+O:3=9				
	Stenosis Spondylolisthesis	Goup1:172participants;age49±11;female:male:111:161;follow-up:32.7 (12-58) Group2:199participants;age50±13;female:male:126:73;follow-up:32.7 (12-58)	RCS	1.2.3.5.6.7.10	S:3+C:2+O:3=8				
	Lumbar degenerative	Goup1:43participants;age50.0±5.4;female:male:21:22;follow-up:1year	RCS	2.3.4.	S:3+C:2+O:3=8				
	disease Spondylolisthesis	Group2:43participants;age50.5±4.6;female:male:19:24;follow-up:1year Goup1:48participants;age:44.6;female:male:24:24;follow-up:6-12months	RCS	1.2.3	S:3+C:2+O:3=8				
	Single-level lumbar degenerative disease	Group2:48participants;age45.3;female:male:16:32;follow-up:6-12months Goup1:43participants;age:55(36-79);female:male:28:15;follow-up:21months(18-26)	RCS	1.2.3.6.10.14	S:4+C:2+O:2=8				
	Lumbar degenerative disease	Group2:104participants;age52(36-78);female:male:67:37;follow-up:23months(18-28) Goup1:35participants;age:52.2±3.3;female:male:10:25;follow-up:NA	PCS	2.3.10	S:4+C:2+O:1=7				
	Spondylolisth	Group2:35participants;age51.2±3.5;female:male:11:24;follow-up:NA Goup1:23participants;age:55(42-76);female:male:13:10;follow-up:11months(9-22)	RCS	1.2.3.6	S:3+C:2+O:3=8				
0 0 0 1	Lumbar degenerative disease	Group2:26participants;agc54(38-72);female:male:10:16;follow-up:11months(9-22) Goup1:82participants;age:52.4(42-65);female:male:38:44;follow-up:18months(12-28) Group2:76participants;age13:8(46-61);female:male:30:44;follow-up:18months(12-28)	RCS	1.2.3.6.7.10	S:3+C:2+O:3=8				
	Single level lumbar spine degenerative disease	Goup1:22participants;age:49.4±12.1;female:male:15:7;follow-up:12months (6months-24months)	RCS	2.3.5.6.10	S:4+C:2+O:3=9				
Jason S. Cheng2013[74]	Spondylosis+ Spondylolisthesis+ Foraminal	Group2:26participants;agc50.7±11.8;fcmalc:malc:15:11:follow-up:12months (6months-24months) Goup1:250participants;agc53.7±11.5;fcmalc:malc:23:27; Group2:25participants;agc54.3±11.1;fcmalc:malc:11:14;	RCS	2.3.4.7	S:3+C:2+0:3=8				
	stenosis Degenerative	The average follow-up for all patients was5.05±1.4 years Goup1:44participants;age:44±10.1;female:male:25:19;follow-up:3-12months	RCS	2.3.4.7	S:3+C:2+O:3=8				
	instability + Deformitys	Group2:54participants;age45±11.2;female:male:24:30;follow-up:3-12months Goup1:50participants;age:NA;female:male:NA;follow-up:3year	PCS						
	One-segment lumbar disc herniation	Group2:56participants;ageNA;female:male:NA;follow-up:3year Goup1:24participants;age:52.42±8.44;female:male:14:10:follow-up:14.71±1.90	RCS	2.3.4.5.14	S:4+C:2+O:2=8 S:4+C:2+O:1=7				
	Lumbar disc herniation	Group2:24participants;age53.42±9.50;female:male:11:13;follow-up:14.38±1.88 Goup1:19participants;age:39-72;female:male:11:8;follow-up:3-12M		4.6					
	Spondylolisth	Group2:34participants;age41-79;female:male:21:13;follow-up:3-12M Goup1:20participants;age:55.7±8.3;female:male:10:16;follow-up:3-12M	RCS	1.2.3.5.6	S:3+C:2+O:3=8				
Shu Dong Ping2016[79]	Lumbar degenerative disease spondylolisthesis+ Foraminal stenosis	Group2:25participants;age55.4±8.6;female:male:11:15;follow-up:3-12M	RCS	2.3.4.5.7.10	S:3+C:2+O:3=8				
Tang Hong Wei2016[80]	Lumbar degenerative disease	Goup1:20participants,age50.9(27-71);Female:male 10:10follow-up:24.4(14-38months) Group2:25participants,age50.2(36-72);Female:male 13:12Follow-up:24.4(14-38months)	RCS	2.3.6	S:4+C:1+O:2=7				
Tang Fu Xing2015[81]	Discogenic Low Back Pain	Goup1:28participants;age:44.7(37-66);female:male:13:15;follow-up:36months (32-47months) Group2:30participants;age45.5(35-68);female:male:13:17;follow-up:39months (35-51months)	RCS	1.2.3.4.5.6.10	S:3+C:2+O:3=8				
Yan Xiong Wei2016[82]	Lumbar degenerative disease	Goup1:51participants;age:62.8±8.7;female:male:28:23;follow-up:48.7±21.8M Group2:46participants;age61.9±11.3;female:male:25:21;follow-up:48.6±19.7M	PCS	2.3.4.7.14	S:4+C:2+O:2=8				
Intrioperative radiological exp 28bod loss 3Surgury time 4Hospitalization 5VAS 6ODI 7Fusion rate 8Short-form36 9Neurogenic symptom scores 10Postoperative drainage volum 11CRP 10Postoperative drainage volum 11CRP 12CK-MM 13CPK 14Complication	ne al:								
RC: Francourized controlled in the PCS: prospective cohort study: RCS: retosactive cohort study									

#### Table 1. Information of the two groups in the finally included articles

RCS: retrospective cohort study DDD: Degenerative disc diseases S: Selection C:Comparability O: Outco

### 6 Conclusion

Our meta-analysis suggests that compared to TLIF, MIS-TLIF is associated with increased intraoperative radiological exposure but results in significantly less intraoperative blood loss, reduced postoperative drainage volume, shorter hospital stays, and lower overall VAS and ODI scores. Additionally, MIS-TLIF is linked to lower levels of CRP, creatine kinase-MM (CK-MM), and CPK postoperatively. However, no significant differences were observed between the two techniques in terms of operative time, fusion rate, and physical and mental recovery.

### **Article History**

Received: July 3, 2024 Accepted: July 10, 2024 Published: September 30, 2024 References

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# Exploring the Application Effect of SBAR Communication Mode in Emergency Nursing

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### Abstract

**Objective:** To explore the effect of the standardized communication mode (SBAR) in emergency nursing. **Methods:** A total of 116 patients in the emergency department from January 2021 to December 2021 were selected as research subjects. The patients were retrospectively divided into a control group and an observation group based on their order of admission, with 58 cases in each group. The control group received conventional emergency nursing, while the observation group received SBAR-based communication in addition to conventional care. The efficiency indicators of emergency nursing treatment were compared between the two groups. **Results:** The efficiency indicators for emergency nursing treatment (including emergency retention time, emergency reception time, and nursing treatment time) in the observation group were significantly shorter than those in the control group, with statistical significance (P = 0.000). **Conclusion:** The SBAR communication mode can improve the efficiency of emergency nursing treatment and is of great significance for enhancing the quality of emergency care.

Keywords Emergency nursing; SBAR communication mode; Effect

**To Cite This Article** Li ZHANG, et al. (2024). Exploring the Application Effect of SBAR Communication Mode in Emergency Nursing. *Medical Research*, 6(3), 41-46. https://doi.org/10.6913/ mrhk.060304

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

The emergency department is the hospital's direct interface with the outside world and a key area for rescuing critical, severe, and emergency patients<sup>[1]</sup>. Critically ill patients present with complex, critical, urgent, and sudden conditions, requiring close monitoring and challenging transfers<sup>[2]</sup>. Miscommunication is a leading cause of clinical errors, such as misdiagnosis and medical accidents<sup>[3]</sup>. Improving communication between medical staff helps prevent adverse outcomes and fosters harmony and progress within the medical team<sup>[4]</sup>. SBAR is an acronym for "situation," "background," "assessment," and "recommendation." It is a standardized and structured communication model recommended by the World Health Organization, serving as an efficient tool to promote communication and is applicable to all types of information transmission<sup>[5]</sup>. SBAR involves four stages: "situation," "background," "assessment," and "recommendation" <sup>[6]</sup>. It has been adopted and refined in various clinical care units across hospitals, becoming an industry-leading communication model that integrates "model training, model application, and model feedback" <sup>[7]</sup>. Currently, the SBAR communication model is primarily used domestically for condition reporting, communication between medical staff and patients, handovers during nursing shifts, safe patient transfers, and nursing education<sup>[8]</sup>. This model enables nurses to gather more comprehensive information about the patient's condition and implement evidence-based nursing interventions, minimizing adverse events and improving the quality of emergency care<sup>[9]</sup>. This article specifically analyzed the application of the SBAR model in 116 patients in the emergency department from January 2021 to December 2021, and the report is as follows.

### 1 Subjects and Methods

### 1.1 Subject Information

A total of 116 patients in the emergency department where the author worked, from January 2021 to December 2021, were selected as research subjects and were retrospectively divided into a control group and an observation group according to the order of admission, with 58 cases in each group. The patients in the observation group were aged 31 to 70 years, with an average age of (54.0  $\pm$  12.6) years; there were 38 males and 20 females. Reasons for visiting included 38 cases of accidental injuries and 20 cases of acute attacks of underlying conditions. The patients in the control group were aged 30 to 70 years, with an average age of (53.4  $\pm$  12.1) years; there were 36 males and 22 females. Reasons for visiting included 41 cases of accidental injuries and 17 cases of acute attacks of underlying conditions. The data from both groups were included in the statistical analysis, and the differences were not statistically significant (P > 0.05).

### 1.2 Case Inclusion Criteria

All 116 patients were admitted to the emergency department of the author's unit. Patients were admitted to the hospital either by ambulance or on their own. All patients were conscious and able to communicate with medical staff. Patients transferred for treatment or those with special

conditions (such as mental illness) were excluded.

### 1.3 Methods

The patients in the control group received conventional emergency nursing, which mainly involved routine disease monitoring, drug interventions, health education, and specialist followup. The patients in the observation group received SBAR-based care in addition to conventional methods.

1. Form an SBAR team: Relevant work plans, personnel responsibilities, and other matters were formulated. Based on the characteristics of diseases in the emergency department and relevant literature from the database, an SBAR mode specification was developed. This included nursing teaching courseware for disease treatment, clinical application examples, and other materials. Team members were trained through theoretical instruction, simulation case drills, skill demonstrations, and were only allowed to join the team after passing an assessment.

### 2. Create the SBAR standard form:

- The **S module** includes detailed information such as the patient's name, gender, age, time of visit, and preliminary diagnosis.
- The **B module** covers the patient's chief complaint, past medical history, current medical history, and abnormal examination results.
- The **A module** includes the patient's vital signs, skin condition, infusion and transfusion details, and pipeline management.
- The **R module** records the nurse's detailed judgment of the patient's condition, changes in vital signs, lesion description, airway secretions, and pipeline status.
- 3. Specific application of SBAR: When receiving patients in the emergency department, the SBAR mode was immediately integrated into the nursing process. This included the steps of collecting patient information, tracking their condition, assessing the patient's status, implementing nursing interventions, and conducting shift handovers. This ensured continuity, integrity, and an evidence-based approach throughout the entire nursing process.

### 1.4 Therapeutic Indicators

The efficiency indicators of emergency nursing treatment for the two groups of patients were recorded, including emergency reception time (the time from when the patient enters the emergency room to the start of nursing treatment), emergency retention time (the total time the patient stays in the emergency room), and nursing treatment time (the total time the patient receives nursing care in the emergency room). A statistical comparison was then conducted.

#### 1.5 Statistical Analysis

All the data in this study were processed using SPSS version 24.0, with a statistical significance threshold of P < 0.05. Categorical data were expressed as "n (%)" and tested using the  $\chi^2$  test. Continuous data were expressed as  $\bar{x} \pm s$  standard deviation (SD), and pairwise comparisons were performed using the t-test for grouped samples. When the variances of the two groups were not homogeneous, the t' test was used.

### 2 Results

The emergency retention time, emergency reception time, and nursing treatment time for patients in the observation group were shorter than those in the control group, with statistically significant differences (P = 0.000). See Table 1.

Table 1: Comparison of the efficiency of emergency nursing treatment between the two groups of patients ( $\bar{x} \pm$  SD)

Group	Number of cases	Emergency reception time (min)	Emergency retention time (min)	Nursing treatment time (min)
Observation group	58	$10.6 \pm 3.4$	$31.4 \pm 5.8$	23.2±5.1
Control group	58	$18.1 {\pm} 4.8$	38.4±7.7	$29.3 \pm 8.4$
T Value	-	-9.710*	-5.530*	-4.727*
P Value	-	0.000	0.000	0.000

*Note*: \* indicates that the data variance for this group is not homogeneous, and the result uses the t' value.

### 3 Discussion

Nursing work in the emergency department is characterized by a high level of busyness and urgency. This is especially true when managing the initial diagnosis and rescue of critically ill patients, where patient diagnoses are often unclear, conditions are unknown, and they can change rapidly. If timely and proper treatment is not administered, it may negatively impact the patient's treatment and safety<sup>[10]</sup>. Therefore, how to further improve rescue and care in the emergency department is a key area of focus.

The SBAR mode is a structured communication method that has been applied in clinical nursing practice in recent years. Originally, it was widely used in fields such as aviation and was later introduced into medical treatment and care<sup>[11]</sup>. In nursing, the SBAR mode ensures the accurate transmission of handover information, optimizes processes, and follows "best practice" procedures while being cost-effective. The handover system reflects the link management of nursing work overseen by nursing managers<sup>[12-15]</sup>, improves nursing efficiency, reduces the frequency of adverse events, and serves as a fast, effective, and structured communication tool<sup>[16]</sup>.

The application of the SBAR mode in the rescue and care of emergency department patients involves developing a standardized communication framework for disease treatment. All nursing staff undergo training and assessment to ensure they can competently perform emergency care and rescue. This approach saves time during critical situations and improves the overall efficiency of rescue efforts, which is of great significance for the subsequent treatment of patients.

From the results of this study, the efficiency indicators for emergency care and treatment (emergency reception time, emergency retention time, and nursing treatment time) were significantly shorter in the observation group compared to the control group, with P < 0.05. This demonstrates that SBAR can enhance the efficiency of emergency care and treatment.

In conclusion, the application of SBAR in the emergency department improves the efficiency of care and treatment and holds significant importance for the subsequent rescue of patients.

#### Article History

Received: June 15, 2024 Accepted: July 12, 2024 Published: September 30, 2024 References

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# Diagnostic Accuracy of Colposcopy in Cervical Intraepithelial Neoplasia and Its Influencing Factors: A Retrospective Study

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### Abstract

**Objective**: To evaluate the diagnostic accuracy of colposcopy for cervical intraepithelial neoplasia (CIN) and identify influencing factors. **Methods**: A retrospective analysis of 493 cases where colposcopy and biopsy were performed, with pathological confirmation as the gold standard. Sensitivity, specificity, positive and negative predictive values of colposcopy were assessed, along with concordance between colposcopy and biopsy. Factors like HPV types, TCT results, transformation zone types, and lesion size were examined for their impact on accuracy. Logistic regression was used to identify key influencing factors. **Results**: Colposcopy showed a sensitivity of 78.11%, specificity of 81.06%, positive predictive value of 91.86%, and negative predictive value of 57.53%, with a Kappa value of 0.525 (P < 0.001). The agreement between colposcopy and biopsy was 70.79%. HPV subtype, transformation zone type, age, and lesion size influenced diagnostic accuracy. Logistic regression identified types II and III transformation zones as independent risk factors for diagnostic errors. **Conclusion**: Colposcopy has limitations in diagnosing CIN. Clinical judgment, supplemented by random biopsy, is crucial to avoid omissions, particularly in patients with unsatisfactory colposcopy results.

Keywords Tetanus; Muscle Spasms; Wound Management; Clostridium tetani; Immunization To Cite This Article Yehong HUANG, et al. (2024). Diagnostic Accuracy of Colposcopy in Cervical Intraepithelial Neoplasia and Its Influencing Factors: A Retrospective Study. *Medical Research*, 6(3), 47-57. https://doi.org/10.6913/mrhk.060305

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

Cervical cancer is a common malignant tumor in women that poses a serious threat to women's health. Statistically, approximately 600,000 new cases of cervical cancer are diagnosed globally each year, representing 5% of all new cancer diagnoses<sup>[1]</sup>. In 2020, China recorded about 120,000 new cases, constituting one-fifth of the global total<sup>[2,3]</sup>.

The clinical signs of precancerous cervical lesions and early-stage cervical cancer are subtle and typically detectable only through screening. Currently, HPV testing and/or cytology form the cornerstone of cervical cancer screening. Colposcopy is used to further diagnose and pinpoint lesions, with biopsy under colposcopic guidance providing a definitive diagnosis or exclusion of cervical cancer and precancerous conditions, thus guiding treatment and follow-up care.

Despite its significance in cervical cancer prevention and treatment, recent studies have highlighted colposcopy's suboptimal accuracy in identifying precancerous and early-stage cervical cancer. These studies note the risks of both missed and erroneous diagnoses<sup>[4-6]</sup>. This study assesses the diagnostic accuracy of colposcopy for cervical intraepithelial neoplasia (CIN) and explores factors associated with improving its clinical utility.

### 1 Materials and Methods

### 1.1 General Information

Colposcopic examinations were conducted in the colposcopy room of Longgang District People's Hospital, Shenzhen, from January 1, 2022, to December 31, 2022. The initial assessments were deemed "satisfactory." Biopsies were performed on lesions identified by colposcopy or through random biopsies after informed consent was obtained from patients with clinical indications but no colposcopic abnormalities.

### 1.1.1 Inclusion criteria

- 1. Women aged 25-65 years with a history of coitus.
- 2. Cytologic screening results and HPV-DNA test results available prior to colposcopy.
- 3. Pathological diagnosis results of cervical biopsy guided by colposcopy.

#### 1.1.2 Exclusion criteria

- 1. Patients with a history of cervical surgery or hysterectomy.
- 2. Patients with a history of treatment for cervical precancerous lesions.
- 3. Non-cervical squamous epithelial lesions or cervical cancer cases.

### 1.2 Colposcopy and Biopsy

Colposcopies were conducted by a specialist and reviewed by two or more associate director physicians at our hospital using an electronic colposcope (Leisegang Feinemchanik-OP; Leisegang

3ML/F.F.P.). Observations focused on changes in the cervical epithelium and blood vessels at varying magnifications, particularly in the transformation area. If no suspicious lesions were observed under direct colposcopic view and clinical indications were present, biopsies were randomly taken from the transformation area at the 3, 6, 9, and 12 o'clock positions. If the transformation area was not fully exposed, or if lesions extended into the cervical canal, endocervical curettage (ECC) was performed. Colposcopy diagnoses were classified as: normal cervix, low-grade intraepithelial neoplasia, high-grade intraepithelial neoplasia, and suspicious carcinomato-sis<sup>[7]</sup>.

### 1.3 Pathological Examination

All cervical tissue specimens underwent pathological examination by our hospital's qualified pathologists. Diagnoses were reviewed and finalized by two senior pathologists. Following the WHO 2014 classification of female reproductive tumors, a secondary classification system was recommended, distinguishing between LSIL and HSIL. LSIL corresponds to CIN1, while HSIL typically includes most cases of CIN2 and CIN3. CIN2 was triaged using immunohistochemical P16 staining; negative results were treated as LSIL, and positive results were managed as HSIL.

### 1.4 Statistical Approach

SPSS 22.0 software was utilized for data coding and statistical analysis. A Chi-square test was used to analyze the data, and multivariate logistic regression was employed to identify statistically significant influencing factors, isolating independent risk factors that impacted the accuracy of colposcopy diagnoses. The threshold for statistical significance was set at  $\alpha = 0.05$ , with P < 0.05 deemed significant.

### 2 Results

### 2.1 Accuracy of Colposcopy in Diagnosing CIN

This study included 493 patients with a median age of 37 years (range: 25-65 years). Of these, 426 patients (86.41%) were under 50 years old, and 67 patients (13.59%) were over 50. There were 63 cases (12.78%) of high-grade cervical lesions and 430 cases (87.22%) of non-high-grade lesions. HPV16/18 was positive in 241 cases (48.88%), and non-HPV16/18 was positive in 252 cases (51.12%).

Regarding the transformation zone type, there were 325 cases (65.93%) of type I, 117 cases (23.73%) of type II, and 51 cases (10.34%) of type III. Cervical lesion area was less than 1/2 in 225 cases (45.64%) and greater than or equal to 1/2 in 268 cases (54.36%).

Diagnostically, 186 cases (37.73%) had a normal cervix (including inflammation), 242 cases (49.09%) had low-grade lesions, and 65 cases (13.18%) had high-grade lesions. The pathological diagnoses were as follows: normal cervix (including inflammation) in 132 cases (26.67%), CIN1 in 269 cases (54.56%), and CIN2 in 92 cases (18.66%).

variate	Number of patients n (%)
Total number of patients	N=493
age	
<50, n (%)	426 (86.41)
≥50, n (%)	67 (13.59)
TCT results	
High grade lesion, $n (\%)$	63(12.78)
Non-high grade lesions, $n (\%)$	430(87.22)
HPV-DNA results	
HPV16/18, n (%)	241 (48.88)
Non-HPV16/18, n (%)	252 (51.12)
Transformation zone type	
Type 1 transformation zone, $n (\%)$	325 (65.92)
Type 2 transformation zone, $n (\%)$	117 (23.73)
Type 3 transformation zone, $n (\%)$	51 (10.34)
Cervical lesion area	
<1/2	225 (45.64)
$\geq 1/2$	268 (54.36)
Diagnostic results of colposcopy	
Normal cervix, n (%)	186 (37.73)
Low grade lesion, $n$ (%)	242 (49.09)
High grade lesion, $n (\%)$	65 (13.18)
Pathological diagnosis results	
Normal cervix, $n(\%)$	132 (26.77)
Low grade lesion, $n(\%)$	269 (54.56)
High grade lesion, $n (\%)$	92 (18.66)

Table 1 Basic characteristics of the research objects

2.1.1 Sensitivity and Specificity of Colposcopy Using the pathological diagnosis as the gold standard, colposcopy achieved a sensitivity of 78.11%, specificity of 81.06%, positive predictive value of 91.86%, and negative predictive value of 57.53% (Kappa value 0.525, P < 0.001). (Table 2).

Diagnosis by	Pathological dia	gnosis (standard)	total	
colposcopy	positive	negative	— total	
positive	282	25	307	positive prediction rate 91.86%
negative	79	107	186	negative prediction rate 57.53%
total	361	132	493	
	sensitivity 78.11%	specificity 81.06%		

Table 2 The specificity and sensitivity of colposcopy images in the diagnosis of CIN n (%)

\*Kappa value 0.525, P<0.001

### 2.1.1 Concordance Between Colposcopy and Pathological Diagnosis

The overall concordance rate between colposcopy and pathological biopsy diagnosis was 70.79% (349/493; see Table 3).

Diagnosis by		total		
colposcopy	Normal cervix	Low grade lesion	High grade lesion	
Normal cervix	107	65	14	186
Low grade lesion	16	195	31	242
High grade lesion	9	9	47	65
total	132	269	92	493

Table 3 Comparison of colposcopy diagnosis and pathological diagnosis (n)

2.2 Univariate Analysis Affecting Diagnostic Accuracy of Colposcopy Factors such as age, HPV16/18 status, type of cervical transformation zone, and cervical lesion area were identified as influencing the diagnostic accuracy of colposcopy (Table 4).

### 2.2 Multivariate Logistic Regression Analysis on Diagnostic Concordance of Colposcopy

A multivariate logistic regression analysis (full model) was conducted with the dependent variable (0 = concordance, 1 = no concordance), using significant variables (P < 0.05) from the univariate analysis as independent variables. The analysis identified type II (OR = 6.906) and type III (OR = 16.653) transformation zones as independent risk factors affecting the accuracy of colposcopic diagnosis of cervical epithelial neoplasia (see Table 5).

### 3 Discussion

Cervical cancer is a common gynecological malignancy with a well-understood etiology and progression, making prevention feasible. Effective screening for detecting precancerous lesions and ensuring timely interventions is essential for preventing cervical cancer<sup>[8]</sup>. Currently, cervical cytology (TCT) and HPV testing are the primary screening methods<sup>[9-11]</sup>. Positive screening results necessitate colposcopy and colposcopically guided cervical biopsies to confirm diagnoses, guide treatment, and manage cases, which are crucial for preventing and treating cervical cancer<sup>[12]</sup>. Thus, improving the accuracy of colposcopy and biopsy remains a key focus of ongoing research and development.

### 3.1 Role of Colposcopy in Diagnosing CIN

Colposcopy is a crucial intermediary between screening and diagnosis in cervical cancer management. Key metrics such as specificity, sensitivity, positive predictive value, negative predictive

Table 4 Univariate analysis affecting diagnostic accuracy of colposcopy									
risk factor	number of cases(n)	Consistency(n)	inconformity(n)	$\chi^2$ value	<i>P</i> value				
age									
≥50	67	37	30	9.087	0.003				
<50	426	312	114						
HPV16/18									
yes	241	185	56	8.133	0.004				
no	252	164	88						
Cytological test									
High grade lesion	63	43	20	0.225	0.635				
Non-highgrade lesion	430	306	124						
Transformation zone type									
Type 1	325	280	45	115.430	< 0.001				
Type 2	117	55	62						
Type 3	51	14	37						
Cervical lesion area									
<1/2	225	171	54	5.431	0.020				
≥1/2	268	178	90						

value, and the concordance rate between colposcopic and biopsy diagnoses, as well as the risks of over-diagnosis and under-diagnosis, are central concerns in colposcopy practice.

In this study, the diagnostic concordance rate of colposcopy was 70.79%, significantly higher than the approximately 50% accuracy rate reported for direct visual biopsy in the literature<sup>[13]</sup>. For instance, in a study by Hopman et al., 23 experienced colposcopists provided presumptive diagnoses based on colposcopic images and biopsy site selection, achieving a concordance rate of 66.7% between colposcopy and pathology diagnoses<sup>[14]</sup>. Similarly, Benedet et al. reported a 50% concordance rate in a multi-center study involving 84,244 patients across 24 colposcopy centers<sup>[15]</sup>.

Colposcopy improves diagnostic accuracy by detecting small lesions that are invisible to the naked eye. The magnified view and enhanced visualization of the cervical squamo-columnar junction, transformation zone, and iodine-stained morphological changes contribute to this improvement. In this study, colposcopy demonstrated a sensitivity of 78.11%, specificity of 81.06%, positive predictive value of 91.86%, and negative predictive value of 57.53%. These results suggest that colposcopy is highly specific and provides a strong positive predictive value, allowing

influence fac	ctor	β	S.E	Wald	P value	ue OR value		OR (95%CI)	
HPV16/18	yes	Reference				1.000			
HP v 10/18	no	-0.187	0.232	0.652	0.420	0.829	0.526	1.307	
7	type I	Reference				1.000			
Zone of transformation	type II	1.932	0.253	58.235	< 0.001	6.906	4.204	11.344	
transformation	type III	2.813	0.381	54.472	< 0.001	16.653	7.891	35.145	
	<50	Reference				1.000			
age	≥50	-0.245	0.332	0.544	0.461	0.783	0.408	1.501	
Conviced legion and	<1/2	Reference				1.000			
Cervical lesion area	≥1/2	0.289	0.234	1.526	0.217	1.335	0.844	2.110	
constant term		-1.907	0.511	13.921	< 0.001	0.148			

Table 5 Multivariate logistic regression analysis of factors affecting the diagnostic accuracy of colposcopy

effective triage of patients and facilitating early interventions for those diagnosed with cervical intraepithelial neoplasia (CIN).

However, the low negative predictive value of 57.53% highlights a risk of missed or underdiagnosed cases, particularly for low-grade cervical squamous intraepithelial neoplasia. Such lesions often present with subtle or indistinct features, making them difficult to detect and prone to misdiagnosis.

Clinicians must meticulously observe colposcopic images, especially for patients with negative TCT and HPV results or those who lack typical colposcopic features. By combining a thorough analysis of images with patient history and current health status, clinicians can improve diagnostic accuracy and continue to build their diagnostic experience.

### 3.2 Factors Influencing the Diagnostic Accuracy of Colposcopy

This study analyzed several factors that may influence colposcopy outcomes, including HPV detection, cytology, transformation zone type, patient age, and cervical lesion area. The findings showed that the detection of specific HPV subtypes (HPV16/18 positive and non-HPV16/18 positive), transformation zone type, patient age, and cervical lesion area significantly affected the accuracy of colposcopy. However, thin-layer liquid-based cytology results did not significantly impact colposcopy's accuracy in diagnosing CIN.

### 3.2.1 Effect of HPV Subtypes on Colposcopy Accuracy

In this study, 241 cases (48.88%) were in the high-risk HPV16/18 positive group, while 252 cases were in the non-HPV16/18 high-risk group. The diagnostic coincidence rates were 76.76% (185/241) for the HPV16/18 positive group and 65.08% (164/252) for the non-HPV16/18 group.

A significant difference was observed between the two groups ( $\chi^2 = 8.113$ , P = 0.004), confirming that the diagnostic accuracy was significantly higher in the HPV16/18 positive group.

Research by Nam et al.<sup>[16]</sup> suggests that colposcopic lesion size varies with different HPV types, with HPV16 being associated with larger lesions, making them easier to detect. Similarly, Stoler et al.<sup>[17]</sup> found that HPV16/18 infection enhances colposcopy accuracy, likely due to the cytopathic effects of E6 and E7 proteins produced by HPV16/18. These proteins degrade P53 and Rb, leading to chromosome mutations, uncontrolled cell proliferation, and cancer. The cytopathic effects are more easily identifiable during colposcopy, improving diagnostic accuracy.

Additionally, clinicians may subconsciously focus more on HPV16/18 positive cases, further increasing detection rates in this group. Therefore, it is essential to remain vigilant for missed or underdiagnosed cases in patients with non-HPV16/18 positive results.

#### 3.2.2 Effect of Transformation Zone on Diagnostic Accuracy of Colposcopy

Cervical precancerous lesions and cervical cancer commonly occur in the cervical transformation zone. Lesions in type I transformation zones are fully exposed, while those in type II zones can be exposed with instrumental assistance. In contrast, lesions in type III zones may extend into the cervical canal, with some or all of the lesions not clearly visualized. The visibility of lesions directly impacts the examination's accuracy—less exposed lesions are more likely to be missed by colposcopy.

In this study, the coincidence rates of colposcopy with cervical biopsy pathology in type I, II, and III transformation zones were 86.15%, 47.01%, and 27.45%, respectively. The highest rate was observed in type I transformation zones at 86.15%, while the rates for types II and III were below 50% (47.01% and 27.45%). Significant differences in diagnostic accuracy were observed across the various transformation zone types, and these differences were statistically significant (P < 0.001).

Research by Guo Shuang<sup>[18]</sup> indicated concordance rates of 78.73%, 71.52%, and 57.27% for types I, II, and III transformation zones, respectively, with type III showing the lowest accuracy. Similarly, He Yu<sup>[19]</sup> reported concordance rates of 72.46%, 71.3%, and 43.5% for types I, II, and III, highlighting that colposcopy accuracy decreases as the visibility of the transformation zone diminishes.

The lower diagnostic accuracy in type III zones aligns with the findings of Guo Shuang and He Yu, suggesting that reduced visibility in the transformation zone increases the difficulty of performing accurate colposcopy and cervical biopsy, potentially leading to missed diagnoses. Consequently, endocervical curettage (ECC) is essential as an adjunctive diagnostic tool for patients with type II and III transformation zones, where lesions may extend into or be situated entirely within the cervical canal.

#### 3.2.3 Effect of Age on Diagnostic Accuracy of Colposcopy

The average age of menopause is around 50 years. In this study, patients were divided into two groups: those under 50 years and those 50 years or older. The diagnostic concordance rates

of colposcopy were 73.24% and 55.22%, respectively, with a statistically significant difference (P = 0.003). This finding is consistent with other research, such as Costa et al.<sup>[20]</sup>, which suggests that the rate of missed diagnoses in colposcopy is positively correlated with age, particularly in patients over 50, due to reduced visibility of the squamo-columnar junction.

Post-menopause, the cervix tends to shrink and shorten, causing the epithelium at the squamocolumnar junction to recede into the cervical canal, leading to partial or complete obscuration of the transformation zone. Additionally, as age increases, ovarian function declines, estrogen levels decrease, and vaginal tissues atrophy. These changes make unexposed areas harder to visualize, complicating colposcopy and reducing diagnostic accuracy.

### 3.2.4 Effect of Cervical Lesion Area on Diagnostic Accuracy of Colposcopy

This study analyzed the impact of cervical lesion size on colposcopy accuracy. Statistical analysis comparing lesions with an area  $\geq 1/2$  of the cervix to those <1/2 revealed a statistically significant difference in diagnostic accuracy (P = 0.020). Previous studies, such as Pretorius et al.<sup>[21]</sup>, have similarly indicated that colposcopy accuracy correlates with the size of the lesion.

Smaller lesions often present fewer distinctive features under colposcopy, making it challenging to accurately biopsy the affected tissue and increasing the likelihood of a missed diagnosis. This underscores the importance of thorough imaging reviews in clinical practice, even when lesions are small or undetected. Incorporating TCT and HPV testing, along with multi-point random biopsies, may improve the accuracy of pathological diagnoses.

### 4 Limitations

Most prior studies assessing the accuracy of colposcopy have used pathological outcomes from cervical conization specimens as the benchmark for evaluating colposcopy-directed cervical biopsy in diagnosing precancerous lesions. In many studies, the interval between colposcopy-guided biopsy and cervical conization is not well-documented, potentially introducing verification bias. While this study successfully addresses this issue, the literature on this topic remains limited. Although the research perspective is innovative, the methodology may still introduce some bias in the findings.

### 5 Conclusion

In conclusion, colposcopy plays a crucial role in preventing and treating cervical cancer, but it has limitations. To minimize missed diagnoses, it is essential to mitigate inadequate diagnostic assessments and perform random biopsies when necessary. Effective colposcopy examinations should consider factors such as HPV subtypes, transformation zone types, patient age, and other clinical conditions to improve diagnostic accuracy.

### 6 Ethics Statement

This study was approved by the Institutional Ethics Committee of Longgang District People's Hospital of Shenzhen (Ethics Approval Number: 2022093). The data were derived from previous clinical diagnoses and treatments as part of retrospective studies. Medical records and specimens explicitly refused by patients were excluded, and patients were not required to provide written informed consent for data release.

### Funds

LGWJ2022-24

### **Article History**

Received: May 12, 2024 Accepted: June 15, 2024 Published: September 30, 2024 References

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## Epidemiological analysis of 4214 emergency trauma patients in Shenzhen

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### Abstract

**Objective:** To analyze case data of emergency trauma patients from May 2018 to May 2023 in a tertiary care hospital in Shenzhen, summarize the patterns of trauma occurrences, and provide references for developing scientific prevention and control measures for emergency trauma patients. Methods: Clinical data of trauma patients who visited our emergency and disaster medical center from May 2018 to May 2023 were collected. Patients were grouped according to different criteria, including age, gender, time of injury, site of injury, and cause of injury, to analyze the epidemiological trends. **Results**: A total of 4214 emergency trauma patients were included, with 2609 males (62%) and 1605 females (38%), showing a significantly higher number of male patients. The age group primarily affected was 19-45 years old, accounting for 48%, followed by 46–65 years old at 35%. The top three trauma sites were the upper limbs in 1659 patients (40%), lower limbs in 1330 patients (32%), and the chest in 414 patients (10%). Regarding the cause of injury, the top five were falls, heavy object injuries, traffic injuries, crush injuries, and roller crush injuries. Trauma incidents occurred more frequently from April to May and less frequently from January to February each year. Conclusion: The majority of emergency trauma patients were male, and the causes and sites of injury showed clear distribution patterns. These findings provide valuable insights for formulating effective prevention and control measures for emergency trauma patients.

### Keywords Emergency department; trauma; epidemiology

To Cite This Article Meiting TANG ,et al. (2024). Epidemiological analysis of 4214 emergency trauma patients in Shenzhen. *Medical Research*, 6(3), 59-66. https://doi.org/10.6913/mrhk.060306 *Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

Trauma refers to the destruction of human tissues or organs caused by mechanical factors. With the rapid development of industry, agriculture, transportation, and sports, trauma resulting from various accidents is on the rise. Trauma not only has a high incidence but also varies significantly in severity and complexity, potentially endangering the lives of those affected. According to statistics, trauma remains the leading cause of death in people under 45 years of age<sup>[1]</sup>. Unlike many other diseases, trauma is highly preventable and controllable. Therefore, understanding the patterns and characteristics of trauma incidents and implementing timely preventive measures can reduce the harm caused by trauma<sup>[2]</sup>. This article retrospectively analyzes 4214 trauma cases admitted to the Emergency and Disaster Medicine Center of our hospital from May 2018 to May 2023, summarizes the epidemiological trends, and provides a reference for the prevention of trauma in emergency patients.

### 1 Materials and Methods

### 1.1 General Information

**Inclusion criteria**: primary diagnosis of trauma, complete emergency medical records. **Exclusion criteria**: refusal to receive treatment, incomplete data. This study obtained clinical data from 4214 emergency trauma patients who visited the Department of Emergency Surgery at the Emergency and Disaster Medical Center of our hospital from May 2018 to May 2023. The data included age, gender, injury site, and cause of injury.

### 1.2 Grouping Method

Patients were grouped based on different criteria: (1) Age groups: minors ( $\leq$ 18 years), young adults (19–45 years), middle-aged adults (46–65 years), and elderly (>65 years). (2) Injury site: injuries were classified into five categories—craniocervical, chest, spine, pelvis, upper limbs, and lower limbs. (3) Cause of injury: injuries were categorized into 11 types—falls, heavy object trauma, traffic injuries, crushing injuries, falls, sharp instrument injuries, sprains, bruises, assault, blast injuries, and other causes.

### 1.3 Statistical Analysis

Data were entered using Excel 2021 and analyzed with SPSS 19.0 statistical software. Categorical data were expressed as percentages (%) and compared using the  $\chi^2$  test. A value of P < 0.05 was considered statistically significant.

### 2 Results

### 2.1 General Information

In this study, there were 2609 male cases (62%) and 1605 female cases (38%), with a sex ratio of 1.66:1, and significantly more males than females. The age group of emergency trauma patients

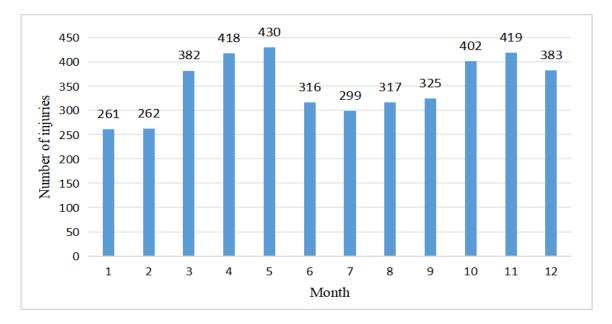
was mainly concentrated between 19 and 65 years old, accounting for 83%, with the 19–45 years age group having the most cases, accounting for 48%, as shown in Table<sup>[1]</sup>.

Age (years)	Male	Female	Total	Proportion
0-18	228	155	383	9%
19 to 45	1295	746	2041	48%
46 to 65	887	593	1480	35%
> 65	199	111	310	7%
Total	2609	1605	4214	100%

 Table 1 Gender and age distribution of emergency trauma patients

### 2.2 Monthly Distribution

The statistical analysis of the monthly distribution of trauma patients showed that there were more trauma patients from April to May each year, accounting for 10%, and fewer trauma patients from January to February, accounting for 6%, as shown in Figure 1<sup>[2]</sup>.



### Figure 1: Distribution Plot of Months of Trauma Events

### 2.3 Trauma Sites and Types

The upper and lower limbs were the most common trauma sites, with 1659 cases (39.37%) in the upper limbs and 1330 cases (31.56%) in the lower limbs, followed by 414 cases (9.82%) in the chest, 366 cases (8.69%) in the spine, 344 cases (8.16%) in the craniocervical region, and 83 cases (1.97%) in the pelvis<sup>[3]</sup>.

### 2.4 Causes of Trauma

The most common cause of injury was falls, accounting for 1659 cases (40.22%), followed by heavy object injuries in 694 cases (16.47%), traffic injuries in 369 cases (8.76%), crush/roller crush injuries in 361 cases (8.57%), sprains in 290 cases (6.88%), bruises in 213 cases (5.05%), sharp instrument injuries in 125 cases (2.97%), beating injuries in 113 cases (2.68%), other causes in 32 cases (0.76%), and blast injuries in 6 cases  $(0.14\%)^{[4]}$ .

### 2.5 Age Distribution of Injury Causes

Falls were the most common injury cause across all age groups. In the 19–45 years age group, the main injury factors were heavy object injuries (409 cases, 9.71%), traffic injuries (192 cases, 4.56%), and crush/roller crush injuries (221 cases, 5.24%). Fall injuries were primarily concentrated in the 19–65 years age group, with 159 cases (3.77%) and 143 cases (3.39%) in the 19–45 and 46–65 years age groups, respectively. There were significant differences in the distribution of injury factors across different age groups ( $\chi^2 = 5164.81$ , P < 0.01)<sup>[5]</sup>.

Table 2 Analys	is of causes	of injury in trau	ma patients of di	fferent ages	
Injurious factors	< 18 years	19 to 45 years	46 to 65 years	> 65 years	Total
Falls	221	641	585	248	1695
Heavy object injury	17	409	262	6	694
Traffic injury	14	192	140	23	369
Crushing/crushing injury	27	221	111	2	361
Fall injury	11	159	143	3	316
Sharps injury	12	57	54	2	125
Sprain	36	169	75	10	290
Crash	35	109	63	6	213
Battery injury	9	62	39	3	113
Blast injury	0	6	0	0	6
Other reasons	1	16	8	7	32
Total	383	2041	1480	310	4214

### 2.6 Trauma Injury Sites

The main injury sites for trauma patients were the upper limbs (1659 cases, 39.37%), lower limbs (1330 cases, 31.56%), chest (414 cases, 9.82%), and spine (366 cases, 8.69%). The distribution of injury sites among different age groups was statistically significant ( $\chi^2 = 4980.06$ , P < 0.01)<sup>[6]</sup>.

Tasiana di mant	< 18	19 to 45	46 to 65	> 65	T-4-1
Injured part	years	years	years	years	Total
Craniocervical injury	49	168	106	21	344
Chest injury	6	177	209	22	414
Spinal injury	9	148	158	51	366
Pelvic injury	2	37	25	19	83
Upper limb injury	229	771	552	107	1659
Leg injury	88	728	424	90	1330
Multiple injuries	0	12	6	0	18
Total	383	2041	1480	310	4214

Table 3 Analysis of injury sites in trauma patients of different ages

### 2.7 Distribution Characteristics of Injury Factors by Injury Sites

The most common injury sites for falls were the upper limbs, lower limbs, and chest. For heavy object injuries, the most common sites were the lower limbs, upper limbs, and chest. Traffic injuries predominantly affected the lower limbs, craniocervical region, and upper limbs. Crush/roller crush injuries primarily involved the upper and lower limbs, while high-altitude falls mainly affected the spine and lower limbs. Significant differences were observed in the distribution of injury factors at different injury sites ( $\chi^2 = 6483.01$ , P < 0.01)<sup>[7]</sup>.

Table 4 Analysis of causes of injury at different injured sites												
Injured part	Falls	Heavy object injury	Traffic injury	Crush/Entrapment	Fall injury	Sharps injury	Sprain	Crash	Battery injury	Blast injury	Other reasons	Total
Craniocervical injury	138	27	84	4	20	4	0	25	37	3	2	344
Chest injury	169	28	48	9	58	1	1	54	36	1	9	414
Spinal injury	165	22	42	3	84	0	21	13	8	0	8	366
Pelvic injury	37	0	19	2	21	0	0	2	0	0	2	83
Upper limb injury	778	254	71	281	56	99	40	54	18	2	6	1659
Leg injury	406	363	103	62	64	21	228	64	14	0	5	1330
Multiple injuries	2	0	2	0	13	0	0	1	0	0	0	18
Total	1695	694	369	361	316	125	290	213	113	6	32	4214

Table 4 Analysis of causes of injury at different injured sites

### 3 Discussion

### 3.1 Regional Characteristics of Trauma in Guangming District

Guangming District is a developing functional district in Shenzhen City, Guangdong Province. In recent years, it has experienced rapid growth, especially in road traffic and the real estate industries. As a result, the trauma incidence in this district differs from other more established regions. This study found that from 2018 to 2023, there were significantly more male trauma patients than female patients, with young adult males (18 to 45 years) being the most affected. This is consistent with similar studies in China<sup>[3]</sup>. The higher incidence among males may be attributed to their involvement in high-risk physical labor, such as construction and transportation. These young males often perform intensive work and engage in high-risk activities but may lack safety experience, making them more susceptible to accidental injuries. Therefore, trauma prevention strategies should prioritize young adult males. Additionally, safety management on construction sites and factories should be strengthened, alongside safety education and publicity efforts.

### 3.2 Temporal Distribution of Trauma Cases

This study also found distinct seasonal patterns in trauma incidence. More trauma patients were reported from April to May each year, while the fewest occurred from January to February. This may be related to Shenzhen's highly mobile population. Trauma events were lowest from January to February, likely because many migrant workers return home during the Chinese New Year festival<sup>[4]</sup>. In contrast, the increase in trauma cases from April to May may be attributed to the rainy season, where wet and slippery conditions, impaired vision, and slower reaction times contribute to a higher likelihood of incidents such as falls and traffic accidents.

### 3.3 Common Injury Sites

The extremities were found to be the most common site of injury. Extremity damage is often the result of fractures in traffic accidents or collisions, as these areas have less fat coverage, making them more prone to injury<sup>[5]</sup>. Wearing appropriate safety harnesses and following operating procedures when performing high-risk tasks can reduce the risk of limb injuries. Strengthening emergency rescue training and on-site first-aid knowledge is urgently needed.

### 3.4 Causes of Trauma by Age Group

Among the causes of injury, falls were the most common, followed by heavy object injuries, traffic accidents, and crushing injuries. A comparison of injury causes across different age groups revealed statistically significant differences (P < 0.05). Falls were especially prevalent in people over 65 years old, with studies estimating that about one-third of the elderly population over 65, and about half of those over 80, experience falls each year<sup>[6]</sup>. This correlation between falls and aging, as well as environmental factors, is consistent with studies from other Chinese cities<sup>[7]</sup>. The National Institute on Aging recommends interventions such as strength and balance exercises, monitoring environmental hazards, regular medical checkups to ensure optimal vision and hearing, and medication management<sup>[8]</sup>. It is crucial to enhance fall prevention facilities and provide education in places where the elderly are active, such as homes, parks, and senior activity centers.

### 3.5 Prevention of Heavy Object Injuries Among Young Adults

Young adults aged 19 to 45 were the most affected by heavy object injuries, a finding consistent with other domestic studies<sup>[9]</sup>. As the primary labor force, many of these workers have limited safety awareness, often neglecting to wear personal protective equipment, failing to check for sharp objects on the items they carry, or lacking coordinated efforts when carrying heavy loads. These factors increase the likelihood of falls and bruises. Therefore, it is essential to strengthen safety training for workers and raise their awareness of safe practices.

### 3.6 Global and Local Impact of Trauma

According to the World Health Organization (WHO), trauma accounts for 10% of global deaths and 16% of disabilities<sup>[10]</sup>. Trauma is a significant public health issue, especially as many trauma patients belong to the social labor force, placing a heavy burden on society and families. Areas with concentrated manufacturing and construction activities are particularly affected, necessitating enhanced safety management and public awareness of safe operations. The type and location of trauma injuries vary across age groups, and tailored preventive measures are required. The findings of this study reflect the epidemiological characteristics of trauma in this region and provide valuable insights for formulating effective trauma prevention and control strategies.

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# Received: May 16, 2024 Accepted: June 24, 2024 Published: September 30, 2024 References

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# The Impact of Aspirin on the Risk of Preeclampsia at Different Gestational Weeks

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### Abstract

Preeclampsia is a common complication during pregnancy that significantly affects both maternal and fetal health. In recent years, aspirin has garnered widespread attention as an important medication for preventing preeclampsia. This review examines the effects of aspirin administration at various gestational stages on the risk of developing preeclampsia, analyzing relevant research findings and theoretical foundations. Additionally, the review discusses the optimal timing and dosage of aspirin in this context. Through a comprehensive analysis of existing literature, this article aims to provide guidance for clinical practice in the prevention of preeclampsia.

**Keywords** Preeclampsia; Aspirin; Gestational Weeks; Risk of Occurrence; Prevention **To Cite This Article** Hang GAO, et al. (2024). The Impact of Aspirin on the Risk of Preeclampsia at Different Gestational Weeks. *Medical Research*, 6(3), 67–78. https://doi.org/10.6913/mrhk. 060307

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

### 1 Introduction

### 1.1 Preeclampsia: Definition and Clinical Manifestations

Preeclampsia is a pregnancy-specific disorder characterized by the onset of hypertension and proteinuria after 20 weeks of gestation. Clinically, it presents with symptoms such as severe headaches, visual disturbances, abdominal pain, and edema. The condition can escalate to eclampsia, which involves seizures and poses significant risks to both mother and fetus, potentially leading to maternal and fetal mortality if left untreated<sup>[1]</sup>. The pathophysiology of preeclampsia is complex, involving placental dysfunction, maternal immune response, and cardiovascular changes. Understanding these clinical manifestations is crucial for timely diagnosis and management, as early intervention can mitigate severe complications.

### 1.2 Epidemiology of Preeclampsia

Epidemiologically, preeclampsia affects approximately 2 8% of pregnancies globally, with a higher prevalence observed in certain populations, such as those with a history of hypertension or obesity<sup>[2]</sup>. The incidence is also influenced by factors such as maternal age, with advanced maternal age correlating with a higher risk of severe manifestations of the disease<sup>[3]</sup>. Additionally, the condition is more prevalent in first-time pregnancies and among women with a family history of preeclampsia. The rising rates of preeclampsia are concerning, particularly in light of increasing maternal age and obesity rates in many countries, underscoring the need for effective preventive strategies.

### 1.3 Aspirin as a Preventive Measure

Aspirin has been widely studied for its potential role in preventing preeclampsia, particularly in high-risk populations. Low-dose aspirin is thought to work by inhibiting platelet aggregation and improving uteroplacental blood flow, thereby reducing the risk of placental ischemia, a key contributor to preeclampsia<sup>[4]</sup>. Current guidelines recommend the use of low-dose aspirin for women at high risk of developing preeclampsia, starting as early as the first trimester<sup>[5]</sup>. The research surrounding the efficacy and safety of aspirin in this context is critical, as it could lead to improved maternal and fetal outcomes.

### 1.4 Purpose of the Review

The purpose of this review is to evaluate the current evidence regarding the effectiveness of lowdose aspirin in preventing preeclampsia, particularly in high-risk populations. By synthesizing the latest findings, this review aims to highlight the importance of early intervention and the potential for aspirin to serve as a valuable tool in the management of preeclampsia, ultimately contributing to better health outcomes for mothers and their infants<sup>[6]</sup>.

# 2 Aspirin as a Therapeutic Approach in the Prevention and Management of Preeclampsia

#### 2.1 Pathogenesis and Risk Factors of Preeclampsia

Preeclampsia (PE) is a complex pregnancy-related disorder characterized by hypertension and proteinuria, affecting approximately 5–8% of pregnancies globally. The pathogenesis of PE is multifaceted, involving maternal, placental, and fetal factors. One key mechanism is the failure of trophoblastic cells to adequately remodel the maternal spiral arteries, leading to placental ischemia and the subsequent release of factors that cause systemic endothelial dysfunction and hypertension. This is further compounded by issues with immune tolerance at the maternal-fetal interface, potentially resulting in an exaggerated inflammatory response that contributes to the clinical manifestations of PE<sup>[7]</sup>.

Risk factors for developing PE include a history of hypertension, obesity, diabetes, and advanced maternal age. Studies have shown that genetic predispositions, such as polymorphisms in genes related to immune response and endothelial function, may also play a role in the development of PE<sup>[8]</sup>. Furthermore, environmental factors such as dietary habits and exposure to toxins have been implicated in the pathogenesis of this condition<sup>[9]</sup>. The interplay between these factors is complex, suggesting that a multifactorial approach is necessary to fully understand and potentially prevent PE.

Recent research has also highlighted the role of microRNAs and long non-coding RNAs in the regulation of gene expression during placentation, which may contribute to the pathophysiology of  $PE^{[10]}$ . Additionally, elevated levels of inflammatory markers, such as S100A9, have been associated with increased secretion of soluble endoglin and IL-1 $\beta$ , further exacerbating hypertension through the activation of the NLRP3 inflammasome<sup>[11]</sup>. Understanding these mechanisms and risk factors is crucial for developing effective prevention and management strategies for PE.

#### 2.2 Mechanisms of Aspirin in Preventing Preeclampsia

Aspirin has been widely studied for its role in the prevention of preeclampsia, particularly in highrisk populations. The primary mechanism by which aspirin exerts its protective effects is through the inhibition of platelet aggregation and the reduction of thromboxane  $A_2$  synthesis, which subsequently improves uteroplacental blood flow and reduces the risk of placental ischemia<sup>[12]</sup>. Low-dose aspirin has been shown to enhance the production of prostacyclin, a potent vasodilator, which counteracts the vasoconstrictive effects of thromboxane<sup>[13]</sup>.

Moreover, aspirin's anti-inflammatory properties play a significant role in modulating the immune response at the maternal-fetal interface. By reducing the levels of pro-inflammatory cy-tokines and promoting an anti-inflammatory environment, aspirin may help maintain immune tolerance and prevent the exaggerated inflammatory response that characterizes PE<sup>[14]</sup>. Recent studies have also indicated that aspirin may influence the expression of genes involved in tro-phoblast cell survival and apoptosis, thereby promoting healthy placentation and reducing the

risk of PE<sup>[15]</sup>.

The timing and dosage of aspirin administration are critical factors influencing its effectiveness. Evidence suggests that initiating low-dose aspirin therapy before 16 weeks of gestation can significantly reduce the incidence of PE in women with identifiable risk factors<sup>[16]</sup>. Additionally, the combination of aspirin with other therapeutic agents, such as apocyanin, has shown promise in enhancing the protective effects against PE by activating key signaling pathways<sup>[17]</sup>. Overall, understanding the multifaceted mechanisms of aspirin in the prevention of preeclampsia is vital for optimizing treatment strategies and improving maternal and fetal outcomes.

## 2.3 Current Research Status of Aspirin Use at Different Gestational Weeks

### 2.3.1 Effects of Aspirin Use in Early Pregnancy

Early pregnancy is a critical period during which the risk of developing complications such as preeclampsia can be significantly influenced by pharmacological interventions. Numerous studies have investigated the effects of low-dose aspirin (LDA) during this stage. Research indicates that initiating aspirin therapy before 11 weeks of gestation can lead to a notable reduction in the incidence of preeclampsia among high-risk populations, particularly in women with a history of hypertensive disorders in previous pregnancies or those with chronic hypertension<sup>[18][19]</sup>. The mechanisms by which aspirin exerts its protective effects include modulation of placental blood flow and reduction of inflammatory markers, which are often elevated in preeclampsia<sup>[20][21]</sup>. A meta-analysis has suggested that early administration of aspirin not only lowers the risk of preeclampsia but also improves perinatal outcomes, including reduced rates of preterm birth and low birth weight<sup>[22]</sup>. However, the optimal timing and dosage remain subjects of ongoing research, with some studies advocating for individualized approaches based on specific risk factors<sup>[23]</sup>. (Figure 1)

## 2.3.2 Risk Assessment in Mid-Pregnancy

As pregnancy progresses into the mid-gestational period, the assessment of risks associated with continued aspirin use becomes essential. During this stage, the potential benefits of aspirin must be weighed against possible adverse effects. Current literature suggests that the use of low-dose aspirin in mid-pregnancy is generally considered safe, but careful monitoring is required, especially for women with preexisting conditions such as diabetes or hypertension<sup>[24][19]</sup>. Studies have shown that mid-pregnancy is characterized by significant physiological changes, including alterations in hemodynamics and placental function, which may influence the efficacy of aspirin<sup>[25]</sup>. Additionally, the risk of bleeding complications, particularly in women with certain co-agulopathies or those undergoing invasive procedures, necessitates a thorough risk assessment<sup>[26]</sup>. Thus, while aspirin continues to be recommended for high-risk populations, clinicians are advised to evaluate individual risk profiles and adjust treatment protocols accordingly<sup>[27]</sup>. (Figure 2)

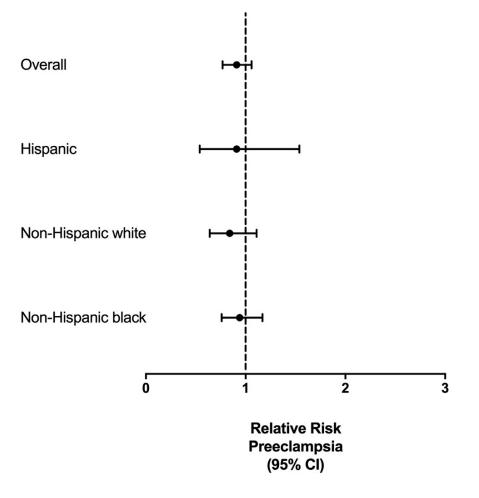


Figure 1: Forest plot of outcomes by ethnicity and race, High-Risk Aspirin (HRA) study There was no significant impact of aspirin in the prevention of preeclampsia among subjects at highrisk, including when stratified by race or ethnicity.CI, confidence interval.Tolcher et al. Impact of ethnicity and race on aspirin for preeclampsia prevention. AJOG MFM 2020.

## 2.3.3 Safety and Efficacy in Late Pregnancy

In late pregnancy, the safety and efficacy of aspirin use require careful consideration, especially as the focus shifts toward managing labor and delivery outcomes. Research indicates that the continuation of low-dose aspirin is generally safe up to the third trimester, but its use should be individualized based on maternal and fetal health status<sup>[28]</sup>. Late pregnancy is often associated with increased risks of placental abruption and postpartum hemorrhage, raising concerns about the potential for aspirin to exacerbate these conditions<sup>[22]</sup>. However, evidence suggests that the benefits of aspirin in preventing preeclampsia and improving placental perfusion may outweigh the risks in selected populations<sup>[27]</sup>. Moreover, ongoing studies are exploring the impact of aspirin on long-term maternal and neonatal outcomes, with preliminary findings indicating that appropriate use may lead to favorable results in terms of maternal blood pressure management and fetal growth parameters<sup>[24][20]</sup>. Thus, while late pregnancy presents unique challenges, aspirin remains a valuable tool in the management of high-risk pregnancies when used judiciously.

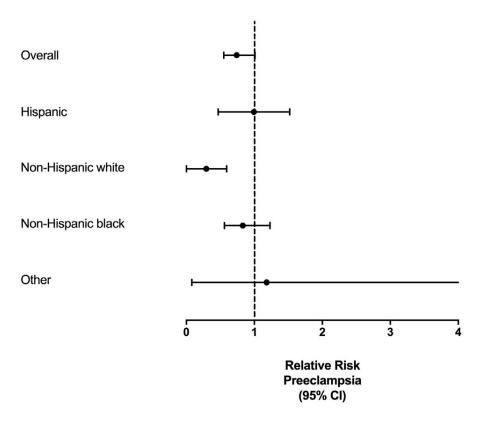


Figure 2: Forest plot of outcomes by ethnicity and race, Low-Risk Aspirin (LRA) study The efficacy of aspirin for prevention among subjects at a low risk of the occurrence of preeclampsiawas observed to be significant only among non-Hispanic white women and not among non-Hispanicblack or Hispanic women.CI, confidence interval.Tolcher et al. Impact of ethnicity and race on aspirin for preeclampsia prevention. AJOG MFM 2020

## 2.4 Current Research Status of Aspirin in the Prevention of Preeclampsia (PE)

The use of low-dose aspirin in the prevention of preeclampsia (PE) has garnered significant attention in both domestic and international research communities. Preeclampsia is a pregnancy complication characterized by high blood pressure and potential damage to other organ systems, particularly the liver and kidneys. The pathophysiology of PE is complex, involving placental dysfunction, inflammatory processes, and endothelial dysfunction. Recent studies suggest that low-dose aspirin may help mitigate these risks by improving placental blood flow and reducing systemic inflammation. For example, a study conducted in China indicated that administering aspirin at a dosage of 75 mg daily effectively reduces the incidence of preeclampsia in high-risk pregnancies, demonstrating its potential as a preventive measure in clinical settings<sup>[29]</sup>.

Internationally, numerous studies have examined the efficacy of low-dose aspirin in preventing PE. One notable study developed a prediction model for first-trimester preterm preeclampsia, highlighting the importance of early intervention with low-dose aspirin in at-risk populations<sup>[30]</sup>. Additionally, a systematic review emphasized aspirin's role in reducing the risk of PE, particularly in women with a history of the condition or other risk factors such as obesity and chronic hypertension<sup>[31]</sup>. The International Federation of Gynecology and Obstetrics (FIGO) has also published guidelines advocating the use of low-dose aspirin in high-risk pregnancies, underscoring its significance in contemporary obstetric care<sup>[32]</sup>.

Furthermore, research into the biological mechanisms through which aspirin exerts its effects on placental health has advanced. Phosphoproteomic studies have provided insights into how aspirin may regulate apoptotic pathways in preeclampsia-like placental models, suggesting a direct impact on placental cellular health<sup>[15]</sup>. These findings underscore the clinical implications of aspirin use and highlight the need for further exploration into its pharmacological mechanisms.

In conclusion, the current landscape of research indicates a promising role for low-dose aspirin in the prevention of preeclampsia. With growing evidence from both domestic and international studies, aspirin appears to be an essential component in managing high-risk pregnancies. Ongoing clinical trials and real-world studies will be crucial in further elucidating the optimal use of aspirin for PE prevention and its long-term effects on maternal and fetal outcomes.

## 2.5 Recommendations from Various National Guidelines on Aspirin for Preeclampsia Prevention

Aspirin has emerged as a key intervention in the prevention of preeclampsia, with various national guidelines endorsing its use for high-risk pregnant women. The American College of Obstetricians and Gynecologists (ACOG) recommends low-dose aspirin (81 mg) starting at 12 weeks of gestation for women with a history of preeclampsia, chronic hypertension, or multiple gestations, among other risk factors. Similarly, the National Institute for Health and Care Excellence (NICE) in the UK supports aspirin prophylaxis for women identified as high-risk, emphasizing its role in reducing the incidence of preeclampsia and its associated complications. In Australia, the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) also advocates for the use of low-dose aspirin in their guidelines, aligning with evidence suggesting its efficacy in high-risk populations. Recent studies underscore the importance of educational interventions to improve adherence to aspirin therapy among pregnant women, highlighting a gap in knowledge that could affect clinical outcomes<sup>[33]</sup>. Overall, the consensus across these guidelines reflects a growing recognition of aspirin's potential benefits in preventing preeclampsia, though variations in recommendations underscore the need for tailored approaches based on individual risk assessments.

## 2.6 Challenges in Clinical Practice and Future Research Directions

The implementation of aspirin for preeclampsia prevention faces several challenges in clinical practice. One significant issue is the underutilization of aspirin prophylaxis, particularly in underserved populations. A study conducted in Sub-Saharan Africa revealed a missed opportunity for aspirin prophylaxis, indicating systemic barriers that prevent high-risk women from receiving appropriate care<sup>[34]</sup>. Additionally, variability in guidelines and the lack of standardized protocols can lead to confusion among healthcare providers regarding when and how to initiate aspirin therapy. The need for effective strategies to improve the utilization of aspirin in high-risk cohorts is evident, as demonstrated by recent research aimed at enhancing adherence through educational

initiatives<sup>[35]</sup>.

## 2.6.1 Limitations of Existing Research

Despite the growing body of evidence supporting aspirin's role in preeclampsia prevention, existing research has notable limitations. Many studies are observational and may be subject to biases, such as selection bias, which can affect the reliability of the findings. Furthermore, there is a lack of consensus on the optimal dosage and timing for aspirin initiation, with some studies suggesting that higher doses may be more effective than lower ones<sup>[36]</sup>. Additionally, the generalizability of findings is often limited to specific populations, raising questions about the applicability of results across diverse demographic groups. These limitations highlight the necessity for more robust, randomized controlled trials to clarify the role of aspirin in various at-risk populations.

## 2.6.2 Future Research Needs and Potential Directions

Future research should focus on addressing the gaps identified in existing studies, particularly through well-designed randomized controlled trials that explore the efficacy and safety of different aspirin dosages and regimens. Investigating the biological mechanisms underlying aspirin's protective effects against preeclampsia could also provide valuable insights that inform clinical practice. Moreover, research should prioritize understanding the socio-economic and cultural factors that influence adherence to aspirin therapy among high-risk populations, as this knowledge could guide the development of tailored interventions. The incorporation of technology, such as mobile health applications, may also enhance patient education and compliance<sup>[37]</sup>.

## 2.6.3 Development and Promotion of Clinical Guidelines

The formulation and dissemination of clinical guidelines for aspirin use in preeclampsia prevention must be a collaborative effort involving obstetricians, researchers, and public health officials. Guidelines should be regularly updated to reflect new evidence and should emphasize the importance of individualized risk assessment in determining aspirin therapy. Furthermore, strategies to promote awareness and education among healthcare providers and patients are crucial for improving adherence to guidelines. Engaging stakeholders in the guideline development process can enhance acceptance and implementation in clinical settings. Ultimately, the successful integration of aspirin prophylaxis into routine prenatal care hinges on a concerted effort to address the challenges identified and to foster an evidence-based approach to managing preeclampsia risk<sup>[38]</sup>.

# 3 Conclusion

In summary, the effectiveness of aspirin in the prevention of preeclampsia has been well-documented, with numerous studies highlighting its role in reducing the incidence of this serious pregnancy complication. Aspirin, particularly in low doses, has emerged as a critical intervention for high-risk populations, such as those with a history of preeclampsia, chronic hypertension, or other

relevant risk factors. While the benefits of aspirin in mitigating the risk of preeclampsia are evident, the timing of administration is equally crucial.

The analysis of risks and benefits associated with aspirin use at various gestational ages reveals a nuanced landscape. Early initiation of aspirin therapy—ideally before 16 weeks of gestation has shown the most promise in reducing the risk of preeclampsia. However, the potential side effects, such as gastrointestinal bleeding or allergic reactions, must also be carefully considered in the risk-benefit assessment. This highlights the need for personalized treatment approaches, taking into account individual patient histories and risk profiles.

As we move forward, it is essential to balance the various findings from existing research while acknowledging the heterogeneity of study populations. The variations in methodology, dosages, and gestational timing across studies can lead to conflicting results. Future research should focus on large-scale, multicenter trials that standardize these variables to provide clearer guidelines. Additionally, the exploration of biomarkers that could predict which patients will benefit most from aspirin therapy may enhance clinical decision-making.

In clinical practice, it is imperative to integrate these findings into patient care, ensuring that healthcare providers are well-informed about the potential benefits of aspirin in preventing preeclampsia while also considering the associated risks. Education on the importance of early screening and personalized care pathways will empower practitioners to make informed decisions in collaboration with their patients.

In conclusion, while aspirin represents a promising strategy for the prevention of preeclampsia, ongoing research and careful consideration of individual risk factors will be essential in optimizing outcomes for pregnant individuals. The path forward should prioritize clarity in research findings and a commitment to evidence-based practice, ultimately aiming for improved maternal and fetal health.

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Received: May 29, 2024 Accepted: June 25, 2024 Published: September 30, 2024 References

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# The Impact of Aspirin on the Risk of Preeclampsia at Different Gestational Weeks

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#### Abstract

Preeclampsia is a common complication during pregnancy that severely impacts both maternal and fetal health. In recent years, competing risk models have emerged as a novel statistical method increasingly used to investigate the risk factors and prevention strategies associated with preeclampsia. This review summarizes the current applications of competing risk models in preeclampsia research, emphasizing their value in risk assessment, preventive interventions, and clinical decision-making. Additionally, it highlights future research directions that could further enhance the understanding and management of this condition.

**Keywords** competing risk models; preeclampsia; prevention; application value; risk assessment **To Cite This Article** Hang GAO, et al. (2024). The Impact of Aspirin on the Risk of Preeclampsia at Different Gestational Weeks. *Medical Research*, 6(3), 79–90. https://doi.org/10.6913/mrhk. 060308

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

## 1 Introduction

Preeclampsia is a pregnancy-specific hypertensive disorder characterized by new-onset hypertension and proteinuria, typically occurring after the 20th week of gestation. It poses significant risks to both maternal and fetal health, including the potential for severe complications such as eclampsia, placental abruption, and fetal growth restriction. The clinical importance of preeclampsia cannot be overstated, as it affects approximately 2-8% of pregnancies globally, making it a leading cause of maternal and perinatal morbidity and mortality<sup>[1]</sup>. Early identification and management of at-risk women are crucial for improving outcomes, which has led to the development of various risk assessment strategies.

Traditional methods for assessing the risk of preeclampsia have included clinical history, physical examination, and basic laboratory tests. However, these approaches often exhibit limitations in sensitivity and specificity, leading to either false reassurance or unnecessary interventions<sup>[2]</sup>. For instance, relying solely on maternal demographics or previous pregnancy history may overlook significant biomarkers that could indicate a higher risk of developing the condition. As such, there is a pressing need for more robust and accurate risk prediction models that can effectively stratify women based on their individual risk profiles.

In recent years, the concept of competing risk models has gained traction in the medical research community. These models account for the presence of multiple potential outcomes that can occur simultaneously, which is particularly relevant in the context of preeclampsia. By incorporating competing risks, researchers can better understand the interplay between various factors that influence the development of preeclampsia and other pregnancy complications. This approach allows for a more nuanced analysis of risk factors and outcomes, ultimately leading to improved clinical decision-making and patient management<sup>[3]</sup>. The rise of competing risk models represents a significant advancement in the field of obstetrics and gynecology, offering new insights into the complexities of pregnancy-related disorders.

# 2 Advancements in Risk Assessment and Prevention of Preeclampsia: The Role of Competing Risk Models and Future Research Directions

#### 2.1 Basic Principles of Competing Risk Models

Competing risks refer to situations in survival analysis where an individual can experience one of several different events, each of which precludes the occurrence of the other events. In clinical research, this is particularly relevant in scenarios involving multiple causes of failure, such as cancer studies where patients may die from cancer or from other causes, such as cardiovascular disease or secondary malignancies. The presence of competing risks complicates the interpretation of survival data, as traditional survival analysis methods, which assume that censoring is the only risk, can lead to biased estimates of survival probabilities. For instance, in a study investigating prognostic factors in patients with osteosarcoma, it was found that using a competing risks approach provided a more accurate survival prediction compared to traditional methods that did not account for the competing nature of death from other causes<sup>[4]</sup>.

Understanding competing risks is essential for clinicians and researchers to make informed decisions regarding treatment and to evaluate the effectiveness of interventions accurately. The mathematical framework for competing risks is built on survival analysis principles but incorporates the presence of multiple potential failure events. The most common approach used is the Fine-Gray model, which estimates the subdistribution hazard function for a particular type of event while accounting for the presence of other competing events. This model allows researchers to derive cumulative incidence functions, which represent the probability of a specific event occurring in the presence of competing risks over time. For example, a study on hepatocellular carcinoma risk in patients with HBV-related cirrhosis utilized a competing risk nomogram to predict outcomes, demonstrating the practical application of these mathematical concepts in clinical settings<sup>[5]</sup>.

By applying these mathematical foundations, researchers can better understand the dynamics of different risks and their implications for patient management. Competing risk models are an extension of traditional survival analysis, which typically focuses on the time until the occurrence of a single event. In contrast, competing risk models acknowledge that patients may experience different events that can influence the probability of the primary event of interest. This relationship is crucial in fields such as oncology, where patients often face multiple potential outcomes.

For instance, a study on the survival probability of patients with sickle cell anemia illustrated how competing risks can provide a more nuanced understanding of patient outcomes compared to conventional survival analysis techniques<sup>[6]</sup>. By incorporating competing risks into survival analysis, researchers can derive more accurate survival estimates and better inform clinical decisionmaking, ultimately improving patient care and outcomes.

#### 2.2 Risk Factors for Preeclampsia

**Genetic predisposition** plays a significant role in the risk of developing preeclampsia. Studies have indicated that women with a family history of preeclampsia are at a higher risk of experiencing this condition themselves, suggesting a hereditary component to its etiology. Specific genetic variants, particularly those associated with endothelial function and immune response, have been implicated in the pathophysiology of preeclampsia. For instance, polymorphisms in genes related to angiogenesis and inflammation may influence a woman's susceptibility to preeclampsia, as these processes are crucial in the development of the placenta and regulation of blood pressure during pregnancy. A cohort study highlighted that women with a history of preeclampsia in previous pregnancies are more likely to experience recurrence, reinforcing the genetic aspect of this condition<sup>[7]</sup>. Furthermore, twin studies have revealed that the heritability of preeclampsia is substantial, indicating that genetic factors contribute significantly to the risk of developing this pregnancy complication<sup>[8]</sup>. Understanding the genetic underpinnings of preeclampsia could lead to better screening and preventive strategies for at-risk populations.

**Environmental factors** also play a critical role in the development of preeclampsia. Various studies have identified lifestyle and environmental exposures that may increase the risk of this

condition. For instance, high levels of stress, poor nutrition, and exposure to pollutants have been linked to adverse pregnancy outcomes, including preeclampsia. Research has shown that women living in areas with high air pollution levels may have an increased risk of developing preeclampsia, possibly due to the inflammatory responses triggered by environmental toxins<sup>[9]</sup>. Additionally, socio-economic factors, such as access to healthcare and education, can influence the prevalence of preeclampsia, as disadvantaged populations may face higher risks due to inadequate prenatal care and unhealthy living conditions<sup>[10]</sup>. Furthermore, dietary factors, including high salt intake and low antioxidant consumption, have been associated with increased blood pressure and vascular dysfunction, which are critical in the pathogenesis of preeclampsia. Addressing these environmental influences is essential for reducing the incidence of preeclampsia among pregnant women.

**Pregnancy-related factors** significantly impact the risk of developing preeclampsia. Maternal age, parity, and the presence of multiple gestations are notable contributors. Advanced maternal age, particularly in women over 35, has been linked to a higher incidence of preeclampsia, possibly due to age-related vascular changes and an increased likelihood of pre-existing health conditions<sup>[11]</sup>. Additionally, first-time mothers (nulliparous women) are at a greater risk compared to those who have had previous pregnancies, as the immune system's adaptation to the placenta may be less developed in first pregnancies<sup>[12]</sup>. The risk is further amplified in multiple pregnancies, such as twins or triplets, due to the increased placental mass and associated hemodynamic changes<sup>[8]</sup>. Other factors, such as pre-existing hypertension, obesity, and diabetes, are also significant risk factors for preeclampsia, highlighting the multifactorial nature of this condition. Understanding these pregnancy-related factors can aid healthcare providers in identifying high-risk patients and implementing early interventions to mitigate the risks associated with preeclampsia.

#### 2.3 Application of Competing Risk Models in Preeclampsia Risk Assessment

Competing risk models have emerged as a powerful tool in the evaluation of preeclampsia risk, offering a nuanced approach that accounts for various outcomes that may occur concurrently. These models typically involve the integration of diverse datasets encompassing maternal demographics, clinical history, and biochemical markers. Data collection often includes longitudinal studies, where pregnant women are monitored for risk factors associated with preeclampsia, such as obesity, hypertension, and family history of the condition. For instance, a study highlighted the importance of early identification of risk factors through multi-marker models, significantly enhancing prediction accuracy in high-risk populations, such as those with pregestational conditions or a history of preeclampsia in previous pregnancies<sup>[13]</sup>(Figure 1).

Moreover, the feasibility of universal screening for preeclampsia risk has been investigated, emphasizing the need for standardized protocols in data collection to ensure consistency and reliability across studies<sup>[14]</sup>. By utilizing advanced statistical techniques, researchers can better understand the interplay of various risk factors and their contribution to the onset of preeclampsia, ultimately leading to improved clinical decision-making and patient outcomes.

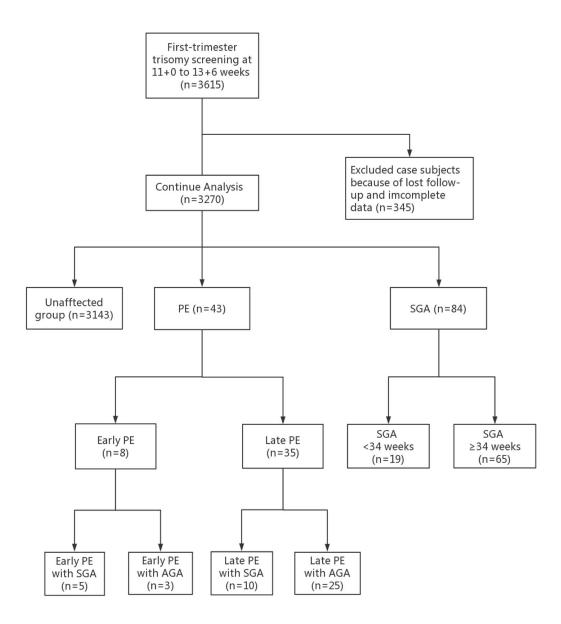


Figure 1: Flowchart of this prospective screening study. Legend: PE = Preeclampsia, SGA = Small-for-gestational-age, AGA = Appropriate-for-gestational-age, n = number

Recent studies employing competing risk models have yielded significant insights into the clinical management of preeclampsia. One critical finding is the identification of specific maternal risk factors that can predict the likelihood of developing early-onset preeclampsia. For example, a population-based cohort study demonstrated that certain pregestational factors, such as advanced maternal age and pre-existing hypertension, substantially increase the risk of both preterm and term preeclampsia<sup>[15]</sup>. The clinical significance of these findings underscores the necessity for tailored monitoring and intervention strategies for at-risk populations.

Furthermore, the application of these models has facilitated the development of targeted preventive measures, such as recommending low-dose aspirin for women identified at high risk. This intervention has been shown to reduce the incidence of preeclampsia<sup>[16]</sup>. This proactive approach not only enhances maternal and fetal outcomes but also optimizes healthcare resource allocation by focusing interventions on those who would benefit the most.

When comparing competing risk models to traditional risk assessment methods, several advantages become evident. Traditional approaches often rely on binary classifications of risk, which can oversimplify the complex nature of preeclampsia and overlook the multifactorial aspects of its etiology. In contrast, competing risk models offer a more comprehensive framework that accommodates multiple potential outcomes, providing a better understanding of the dynamics at play during pregnancy. For instance, while traditional methods may focus solely on the likelihood of developing preeclampsia, competing risk models can account for other pregnancyrelated complications, such as gestational diabetes or preterm birth, which may influence the overall risk profile<sup>[17]</sup>.

This holistic perspective is crucial in clinical settings, where healthcare providers must navigate various risk factors and outcomes to deliver optimal care. Additionally, the predictive accuracy of competing risk models has been shown to surpass that of traditional methods, enhancing clinical decision-making and patient management strategies<sup>[18]</sup>. Ultimately, the integration of these advanced modeling techniques represents a significant advancement in the field of obstetrics, paving the way for more personalized and effective approaches to preeclampsia risk assessment.

#### 2.4 Competing Risk Models in the Prevention of Preeclampsia

Risk stratification is a crucial component in the prevention of preeclampsia, enabling healthcare providers to identify high-risk patients and tailor interventions accordingly. Individualized interventions based on risk assessment can significantly enhance the effectiveness of preventive strategies. Recent studies have highlighted the importance of accurately identifying women at risk for preeclampsia through various factors, including medical history, genetic predispositions, and lifestyle choices.

For instance, the Gottesfeld-Hohler Memorial Foundation emphasizes the necessity of early risk assessment for early-onset preeclampsia, advocating for a proactive approach that integrates personal and familial risk factors into clinical practice<sup>[19]</sup>. Additionally, the implementation of low-dose aspirin as a preventive measure has shown promise, particularly in women identified as high-risk through stratification methods<sup>[20]</sup>. A network meta-analysis further supports the comparative effectiveness of various prophylactic strategies, underscoring the need for personalized care plans that cater to the specific risk profiles of patients<sup>[21]</sup>. This individualized approach not only improves outcomes but also fosters better patient engagement and adherence to preventive measures.

The effectiveness of preventive measures in managing preeclampsia is contingent upon their proper implementation and adherence to guidelines. Evidence suggests that systematic application of prophylactic strategies, such as the administration of low-dose aspirin and lifestyle modifications, can lead to a significant reduction in the incidence of preeclampsia among high-risk populations<sup>[22]</sup>. Furthermore, studies focusing on self-care strategies before and during pregnancy have demonstrated that empowering women with knowledge and resources can enhance the control of risk factors associated with preeclampsia<sup>[23]</sup>. The success of these interventions

is often linked to the quality of risk factor screening and the education provided to expectant mothers, which can lead to early detection and timely management of potential complications.

As healthcare systems continue to evolve, the integration of technology and telemedicine into preventive care presents new avenues for improving access and adherence to preventive measures, ultimately leading to better maternal and fetal outcomes. Optimizing clinical pathways for the prevention of preeclampsia is essential for improving care delivery and patient outcomes.

Clinical pathways that are well-structured and evidence-based can facilitate the standardization of care, ensuring that all patients receive timely and appropriate interventions based on their risk profiles. Recent advancements in technology and data analytics have enabled healthcare providers to refine these pathways, incorporating real-time data to adjust care plans as needed<sup>[11]</sup>. The use of clinical pathways not only streamlines the management of preeclampsia but also enhances interprofessional collaboration, allowing for a more cohesive approach to patient care.

Moreover, optimizing these pathways can lead to improved resource allocation and reduced healthcare costs, as demonstrated by studies focusing on quality improvement initiatives in family medicine residency training<sup>[24]</sup>. As the landscape of maternal healthcare continues to change, ongoing research and evaluation of clinical pathways will be critical in ensuring that they remain effective and responsive to the needs of patients at risk for preeclampsia. (Figure 2)

#### 2.5 Future Research Directions

The advancement of medical research necessitates the continual improvement and innovation of existing models. Current models used in clinical and preclinical research often have limitations that hinder their applicability to real-world scenarios. For instance, the development of more so-phisticated rodent models has been highlighted as a crucial step toward better mimicking human pathophysiological conditions, such as myocardial ischemia and reperfusion injury, which could lead to enhanced understanding and treatment of cardiovascular diseases<sup>[25]</sup>. Additionally, innovative outpatient models are being explored to improve patient care and streamline healthcare delivery<sup>[26]</sup>.

The integration of digital technologies into these models is also essential, as it allows for realtime data collection and analysis, thereby improving the accuracy and reliability of research outcomes<sup>[27]</sup>. Future research should focus on refining these models to ensure they are representative of diverse populations and can accommodate the complexities of multifactorial diseases. This will require interdisciplinary collaboration and a commitment to adopting new technologies and methodologies that can enhance the robustness of research findings<sup>[28]</sup>.

The importance of multicenter studies in medical research cannot be overstated. These studies provide a broader perspective by incorporating diverse patient populations and clinical practices, which enhances the generalizability of research findings. For example, a multicenter study on the efficacy of convalescent plasma transfusion for COVID-19 demonstrated significant variations in treatment outcomes across different centers, underscoring the necessity of multicentric approaches to understanding complex diseases<sup>[29]</sup>.

Additionally, multicenter studies facilitate the pooling of resources and data, leading to more

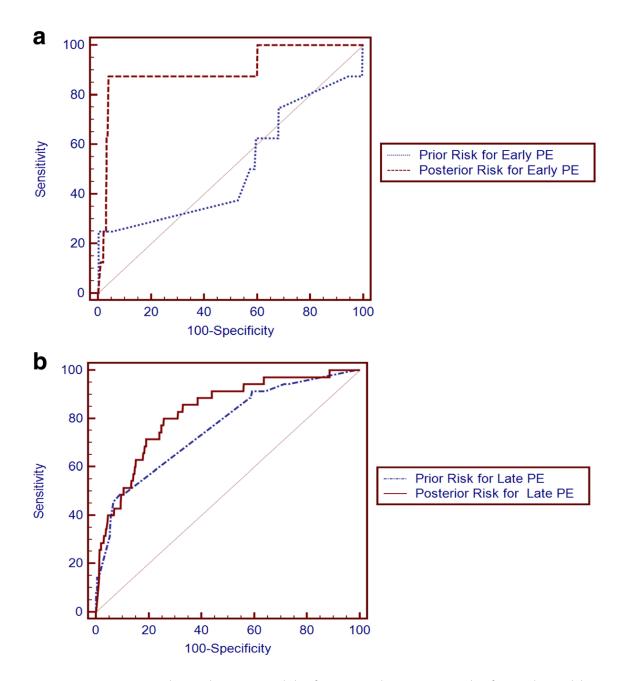


Figure 2: ROC curves with prediction model of prior and posterior risks for early and late PE. Legend: (a) (.....) Prior Risk for early PE, (----) Posterior Risk for early PE; (b) ( - · - · - · ) Prior Risk for late PE, (-----) Posterior Risk for late PE

comprehensive analyses and stronger statistical power. The variation in treatment protocols and patient demographics across centers can provide valuable insights into the effectiveness of various interventions<sup>[30]</sup>. As healthcare becomes increasingly globalized, future research should prioritize multicenter collaborations to address the heterogeneity of patient responses and treatment efficacy, ultimately leading to more tailored and effective healthcare solutions<sup>[31]</sup>.

The emergence of big data has transformed the landscape of medical research, offering unprecedented opportunities for data sharing and analysis. The integration of large datasets can significantly enhance our understanding of disease mechanisms and patient outcomes. For instance, utilizing shared big data has proven effective in identifying liver cancer dedifferentiation markers, which could lead to more targeted therapies<sup>[32]</sup>.

Moreover, the challenges of big data integration in life sciences highlight the need for robust data governance and standardized data models to facilitate effective data sharing<sup>[33]</sup>. As researchers increasingly recognize the human aspect of big data, it is crucial to develop frameworks that ensure ethical data-sharing practices while maximizing the potential benefits of these vast datasets<sup>[34]</sup>. Future research should focus on creating collaborative platforms that promote data sharing among institutions, enabling researchers to leverage collective insights and drive innovation in patient care and treatment strategies<sup>[35]</sup>.

## 3 Conclusion

In conclusion, the development and application of competing risk models represent a significant advancement in the risk assessment and prevention strategies for preeclampsia. These models provide a nuanced perspective, allowing clinicians to consider not only the likelihood of developing preeclampsia but also the potential competing events that may influence the outcome. This multifaceted approach is crucial in tailoring individual patient care and enhancing the scientific basis of clinical decisions.

The integration of competing risk models into clinical practice has the potential to refine risk stratification processes for expectant mothers, thereby improving the identification of those at higher risk for adverse outcomes associated with preeclampsia. By acknowledging the complexities inherent in patient management, these models facilitate more informed dialogues between healthcare providers and patients, ultimately leading to better health outcomes.

However, it is essential to recognize the disparities in research methodologies and findings related to competing risk models. A balanced interpretation of the literature is necessary, as variations in study design, population demographics, and statistical approaches can yield differing results. Future research should focus on standardizing methodologies to enable clearer comparisons and validations of competing risk models across diverse populations.

Moreover, further exploration of the clinical applicability of these models within preeclampsia research is needed. Efforts should be made to encourage collaboration between researchers and clinicians to ensure that the insights gained from these models translate into actionable clinical guidelines. By fostering an environment of interdisciplinary research, we can advance our understanding of preeclampsia and ultimately improve maternal and fetal health outcomes.

In summary, while competing risk models offer promising avenues for improving preeclampsia risk assessment and management, ongoing research and collaboration are vital to harness their full potential. By addressing current gaps and promoting the integration of these models into routine clinical practice, we can pave the way for more effective prevention strategies in the field of obstetrics.

## **Article History**

Received: May 25, 2024 Accepted: June 13, 2024 Published: September 30, 2024 References

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# Medical Research

# **Risk Factors and Preventive Strategies for Surgical Complications Associated with Uterine Fibroids** Kai YAN<sup>1</sup>, Xiuqing ZHANG<sup>2#</sup>, Hang GAO<sup>1</sup>, Xiaolin CHEN<sup>1</sup>, Zhifeng MO<sup>3,\*</sup>

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### Abstract

Uterine fibroids are common benign tumors that often necessitate surgical intervention. However, such procedures can result in complications that have a detrimental impact on patient recovery and quality of life. In this review, we sought to identify and assess risk factors associated with surgical complications in the treatment of uterine fibroids. A comprehensive analysis of clinical studies and relevant literature was conducted to explore common complications, including hemorrhage, infection, and damage to surrounding organs. Furthermore, we examined patient-specific risk factors such as age, comorbidities, and fibroid characteristics. Based on the findings from the literature, we propose preventive strategies to mitigate these risks, including preoperative planning, minimally invasive surgical techniques, and enhanced postoperative care protocols. Additionally, tailored surgical approaches and improved perioperative management can help reduce the incidence of complications, improving patient outcomes and quality of life. These conclusions provide actionable insights for clinicians to optimize treatment plans and minimize risks for patients undergoing surgery for uterine fibroids.

Keywords Uterine fibroids; Surgical complications; Risk factors; Preventive strategies; Clinical research

**To Cite This Article** Kai YAN,et al. (2024). Risk Factors and Preventive Strategies for Surgical Complications Associated with Uterine Fibroids. *Medical Research*, 6(3), 91–102. https://doi.org/10.6913/mrhk.060309

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

## 1 Introduction

Uterine fibroids, also known as leiomyomas or myomas, are the most common benign tumors in women of reproductive age, affecting approximately 70–80% of women by the age of 50<sup>[1]</sup>. They originate from aberrant smooth muscle cells in the smooth muscle layer of the uterus and can vary greatly in size, number, and location, causing a range of symptoms such as heavy menstrual bleeding, pelvic pain, abdominal discomfort, and reproductive problems<sup>[2]</sup>. Despite their benign nature, uterine fibroids can significantly impact a woman' s quality of life and are a leading cause of hysterectomy worldwide<sup>[3]</sup>. The precise etiology of uterine fibroids remains unclear; however, there is consensus that genetic, hormonal, and environmental factors play crucial roles<sup>[4]</sup>. Uterine fibroids are more prevalent among women of African descent than among women of other ethnicities, and women of African descent are more likely to develop fibroids at a younger age and experience more severe symptoms<sup>[5]</sup>. The presence of fibroids can lead to significant morbidity, including anemia due to heavy menstrual bleeding, and can adversely affect fertility and pregnancy outcomes<sup>[6]</sup>.

Surgical intervention remains a cornerstone in the management of symptomatic uterine fibroids. Myomectomy, hysterectomy, and uterine artery embolization are among the most common surgical options<sup>[7]</sup>. Although these procedures can effectively alleviate symptoms and improve quality of life, they are not without inherent risks. Surgical complications such as hemorrhage, infection, and damage to surrounding organs can occur, necessitating a thorough understanding of the risk factors and the development of effective preventive strategies<sup>[8]</sup>. Surgical complications associated with uterine fibroid treatment can significantly impact patient outcomes and healthcare resources. Complications such as hemorrhage, infection, and postoperative adhesions can prolong hospital stays, increase healthcare costs, and adversely affect patient recovery and quality of life<sup>[9]</sup>. Therefore, understanding the risk factors associated with these complications is essential for optimizing surgical outcomes and minimizing patient morbidity<sup>[10]</sup>.

Recent clinical studies have yielded valuable insights into the risk factors and prevention strategies for surgical complications associated with the removal of uterine fibroids. The objective of this clinical review is to provide a comprehensive summary of the most prevalent surgical techniques for the treatment of uterine fibroids, along with an analysis of the associated complications and risk factors. Furthermore, this review outlines strategies for the prevention of these complications.

# 2 Common Types of Surgical Approaches for the Removal of Uterine Fibroids

#### 2.1 Laparoscopic Surgery

Laparoscopic surgery, also known as minimally invasive surgery, has gained considerable popularity as a treatment option for uterine fibroids, mainly due to the numerous advantages it offers over traditional open surgery. This technique involves the use of a laparoscope, a thin, lighted tube with a camera, which allows the surgeon to visualize the pelvic organs on a monitor and perform the procedure through small incisions. Laparoscopic myomectomy is the preferred surgical approach due to its ability to reduce postoperative pain, shorten hospital stays, and facilitate a quicker recovery compared to open myomectomy<sup>[11]</sup>. Studies have shown that laparoscopic myomectomy is an effective intervention for improving health-related quality of life (HR-QoL) and reducing symptom severity in patients with symptomatic uterine fibroids<sup>[12]</sup>. However, the procedure requires a high level of surgical skill and experience, and the risk of complications such as bleeding and infection, although lower than in open surgery, remains a concern<sup>[13]</sup>. Additionally, the size, number, and location of the fibroids can influence the feasibility and success of laparoscopic surgery<sup>[14]</sup>.

## 2.2 Open Abdominal Surgery

Open abdominal surgery, or laparotomy, remains the standard treatment for uterine fibroids, particularly in cases where fibroids are large, numerous, or located in positions difficult to access laparoscopically. This approach involves a larger incision in the abdomen to allow direct access to the uterus. While open myomectomy is highly effective in removing fibroids and alleviating symptoms, it is associated with prolonged hospital stays, increased postoperative pain, and a longer recovery period compared to minimally invasive techniques<sup>[15]</sup>. Despite these drawbacks, open surgery is sometimes necessary to ensure complete removal of fibroids and to manage complications such as severe bleeding<sup>[16]</sup>. Furthermore, studies have indicated that open myomectomy can result in significant improvements in HR-QoL and symptom severity, although it carries an elevated risk of adhesions and other postoperative complications<sup>[17]</sup>.

## 2.3 Uterine Artery Embolization

Uterine artery embolization (UAE) is a minimally invasive procedure that involves the injection of embolic agents into the uterine arteries to block blood flow to the fibroids, causing them to shrink and die. This technique is particularly advantageous for women who wish to avoid surgery and preserve their uterus<sup>[18]</sup>. UAE has been shown to markedly improve HR-QoL and reduce symptom severity in patients with symptomatic uterine fibroids<sup>[19]</sup>. However, this procedure is not without risks. Potential complications include post-embolization syndrome (characterized by pain, fever, and nausea), infection, and, in rare cases, premature ovarian failure<sup>[20]</sup>. Long-term studies have demonstrated that while UAE is effective in the short term, there is a higher likelihood of requiring additional interventions compared to surgical options<sup>[21]</sup>. Nevertheless, UAE remains a valuable alternative for patients seeking a less invasive treatment with a shorter recovery time<sup>[22]</sup>.

# 3 Complications Associated with the Surgical Removal of Uterine Fibroids

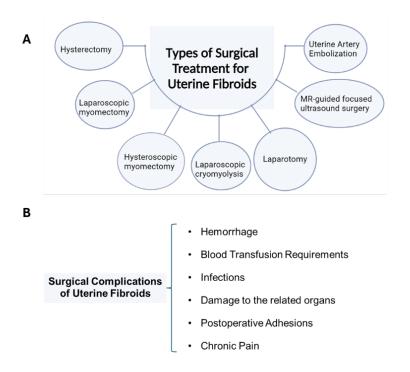


Figure 1. Types of surgical treatment for uterine fibroids and the associated complications.

## 3.1 Hemorrhage and Blood Transfusion Requirements

Hemorrhage is one of the most common and significant complications associated with uterine fibroid surgery. The risk of excessive bleeding is particularly high during procedures such as myomectomy and hysterectomy due to the vascular nature of the uterus and the fibroids themselves. Studies have shown that intraoperative blood loss can be substantial, often necessitating blood transfusions to manage the patient's hemodynamic status. For instance, a study conducted in Tanzania reported that 19.1% of women undergoing hysterectomy for uterine fibroids required a blood transfusion, highlighting the prevalence of this complication<sup>[9]</sup>. The need for transfusion not only increases the complexity and cost of the surgical procedure but also poses additional risks of complications, including transfusion reactions and infections. To mitigate the risk of excessive bleeding, it is recommended to optimize hemoglobin levels prior to surgery, utilize intraoperative hemostatic agents, and employ meticulous surgical techniques to control bleeding<sup>[8]</sup>.

## 3.2 Infection

Another significant postoperative complication is infection at the surgical site following uterine fibroid surgery. These infections can range in severity from superficial wound infections to more severe intra-abdominal infections, including pelvic abscesses and peritonitis. The incidence of postoperative infections can be influenced by several factors, including the duration of surgery, the patient's baseline health status, and the presence of comorbid conditions such as diabetes. A study from Haiti emphasized the significant impact of infections on the quality of life and recovery of women undergoing surgery for uterine fibroids, with a notable percentage of patients experiencing postoperative infections<sup>[5]</sup>. Preventive measures such as prophylactic antibiotics, strict aseptic techniques, and careful postoperative monitoring are essential to reduce the risk of infections<sup>[23]</sup>.

## 3.3 Organ Injury

Injury to adjacent organs is a serious complication that can occur during uterine fibroid surgery, particularly during complex procedures like myomectomy and hysterectomy. The bladder, ureters, and intestines are susceptible to injury due to their proximity to the uterus. Such injuries can lead to significant morbidity, including urinary and gastrointestinal complications. A population-based study in Korea highlighted the long-term risks associated with organ injury during myomectomy, emphasizing the need for careful surgical planning and technique<sup>[3]</sup>. The use of advanced imaging techniques preoperatively and intraoperative guidance can help in identifying and preserving these vital structures<sup>[24]</sup>.

## 3.4 Postoperative Adhesions and Pain

Postoperative adhesions and chronic pain are common complications following uterine fibroid surgery. Adhesions may form as a consequence of surgical trauma and subsequent inflammation, leading to chronic pelvic pain, bowel obstruction, and infertility. Chronic pain, on the other hand, can significantly affect the patient's quality of life and may require long-term management strategies. A systematic review identified several modifiable risk factors for the development of postoperative adhesions, including surgical technique and the use of adhesion barriers<sup>[25]</sup>. Effective pain management protocols, including the use of multimodal analgesia and minimally invasive surgical techniques, can help reduce the incidence and severity of chronic pain<sup>[26]</sup>.

## 4 Risk Factors

## 4.1 Patient Characteristics

Patient characteristics, including age, body mass index (BMI), and the presence of comorbidities, significantly influence the risk of complications following uterine fibroid surgery. Advanced age is associated with an increased risk of perioperative complications, including elevated rates of bleeding and infection<sup>[27]</sup>. Additionally, there is substantial evidence that obesity, as indicated by a high BMI, is a well-documented risk factor for surgical complications. Obese patients are more likely to experience longer operative times, increased blood loss, and higher rates of wound infections<sup>[28]</sup>. Comorbid conditions such as diabetes, hypertension, and cardiovascular diseases further complicate the surgical landscape. These conditions can impair wound healing, increase the risk of thromboembolic events, and exacerbate intraoperative and postoperative complications<sup>[29]</sup>. Therefore, a thorough preoperative assessment of these patient characteristics is crucial for risk stratification and planning appropriate perioperative management strategies.

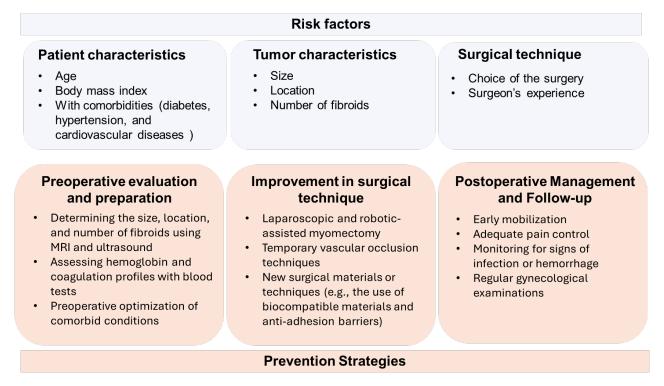


Figure 2. Risk factors and preventative strategies for surgical complications of uterine fibroids .

#### 4.2 Tumor Characteristics

The characteristics of the fibroids themselves, including size, location, and number, are critical determinants of surgical risk. The presence of larger fibroids is associated with increased surgical complexity, longer operative times, and higher intraoperative blood loss<sup>[30]</sup>. The location of the fibroids also plays a significant role. For example, fibroids located near vital structures such as the bladder or bowel increase the risk of organ injury<sup>[31]</sup>. Multiple fibroids can complicate the surgical procedure, making complete resection more challenging and increasing the likelihood of residual disease<sup>[32]</sup>. Preoperative imaging and careful surgical planning are essential to address these challenges and minimize the risk of complications.

## 4.3 Surgical Technique

The selection of surgical technique and the surgeon' s experience are pivotal in determining the outcome of uterine fibroid surgeries. Minimally invasive techniques, including laparoscopic and robotic-assisted surgeries, have been linked to reduced blood loss, shorter hospital stays, and quicker recovery times compared to open surgeries<sup>[33]</sup>. However, the extent to which these benefits are realized depends on the surgeon' s expertise and experience with these techniques. Surgeons with extensive experience in minimally invasive procedures tend to have lower complication rates and better outcomes<sup>[34]</sup>. Conversely, less experienced surgeons may face higher rates of conversion to open surgery, increased operative times, and higher complication rates<sup>[35]</sup>. Continuous training and adherence to standardized surgical protocols are essential to optimize

surgical outcomes and minimize risks.

## 5 Current Status and Challenges of Prevention Strategies

#### 5.1 Preoperative Evaluation and Preparation

Preoperative evaluation and preparation are crucial steps in minimizing the risk of complications during and after uterine fibroid surgery. Comprehensive preoperative assessments, including imaging studies such as MRI and ultrasound, help in accurately determining the size, location, and number of fibroids, which are essential for surgical planning<sup>[36]</sup>. Additionally, preoperative blood tests to assess hemoglobin levels and coagulation profiles are necessary to anticipate and manage potential intraoperative bleeding<sup>[37]</sup>. Preoperative optimization of comorbid conditions, such as diabetes and hypertension, is also critical, as these conditions can increase surgical risks<sup>[38]</sup>. Despite these measures, challenges remain in accurately predicting and mitigating all potential complications, particularly in patients with large or multiple fibroids or those with previous surgical histories<sup>[3]</sup>.

#### 5.2 Improvement in Surgical Technique

Advancements in surgical techniques have significantly contributed to reducing the risk of complications associated with uterine fibroid surgeries. Minimally invasive procedures, such as laparoscopic and robotic-assisted myomectomy, have been shown to reduce intraoperative blood loss, postoperative pain, and recovery time compared to traditional open surgeries<sup>[28]</sup>. The use of temporary vascular occlusion techniques, such as the application of microsurgical vascular clips, has been effective in controlling intraoperative bleeding during the enucleation of large fibroids<sup>[39]</sup>. However, the learning curve associated with these advanced techniques and the availability of specialized equipment can be limiting factors in their widespread adoption<sup>[40]</sup>. Additionally, the risk of morcellation-related dissemination of undiagnosed malignancies remains a concern, necessitating careful patient selection and thorough preoperative evaluation<sup>[37]</sup>.

In a review by Herrmann et al. examining the incidence, risk factors, complications, and prevention of adhesions following laparoscopic myomectomy (LM)<sup>[41]</sup>, it was highlighted that despite the well-known advantages of laparoscopic surgery, such as reduced pain, decreased blood loss, and shorter hospital stays, myomectomy remains a high-risk procedure for adhesion formation. Notably, the data indicated that at least one in five patients developed post-surgical adhesions, which can lead to severe complications like small bowel obstruction, chronic pelvic pain, and impaired fertility. The study also emphasized the importance of surgical experience and minimizing tissue trauma to reduce adhesion formation. Developing effective prevention strategies for post-operative complications of uterine fibroid removal has been a pivotal focus of recent research. For instance, the use of biocompatible materials and anti-adhesion barriers has shown promise in reducing the incidence of post-surgical adhesions<sup>[41]</sup>. Additionally, tissue trauma and the surgeon's experience are critical factors influencing adhesion formation. Therefore, it can be reasonably deduced that the implementation of meticulous surgical techniques and the utilization of advanced laparoscopic instruments can help mitigate these risks.

## 5.3 Postoperative Management and Follow-up

Effective postoperative management and follow-up are essential components of a comprehensive strategy to prevent complications following uterine fibroid surgery. Early mobilization, adequate pain control, and monitoring for signs of infection or hemorrhage are critical in the immediate postoperative period<sup>[38]</sup>. Long-term follow-up, including regular gynecological examinations and imaging studies, is necessary to monitor for the recurrence of fibroids and to manage any late-onset complications such as adhesions or chronic pelvic pain<sup>[42]</sup>. The use of pharmacological agents, such as GnRH analogs, in the postoperative period can help reduce the risk of fibroid recurrence<sup>[28]</sup>. However, adherence to follow-up protocols can be challenging for patients, and there is a need for improved patient education and support systems to ensure compliance<sup>[37]</sup>.

## 6 Future Research Directions

Future research should focus on the long-term outcomes of different surgical approaches and the development of novel materials and techniques to further reduce surgical complications. Studies are needed to evaluate the effectiveness of new anti-adhesion agents and their long-term safety profiles. Moreover, research into personalized medicine approaches, where surgical techniques and preventive measures are tailored to individual patient characteristics, could offer significant advancements in reducing complications. The integration of advanced imaging technologies and robotic-assisted surgeries also holds potential for improving surgical precision and outcomes. Continuous education and training programs for surgeons are essential to keep up with the latest advancements and ensure the highest standards of patient care.

## 7 Conclusion

In summary, uterine fibroid surgery, despite being a prevalent and often necessary intervention for many women, carries the risk of several complications that can significantly impact patient recovery and quality of life. This review has synthesized findings from numerous clinical studies and identified the primary risk factors associated with these surgical complications, as well as proposed effective preventive strategies.

## Article History

Received: May 29, 2024 Accepted: June 27, 2024 Published: September 30, 2024 References

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# Comparative Efficacy of Single-Fraction versus Multi-Fraction Stereotactic Body Radiotherapy for Spinal Metastases: A Meta-Analysis

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### Abstract

**Objective:** This study compares the efficacy of stereotactic body radiotherapy (SBRT) in patients with spinal metastases, focusing on single-fraction (SF-SBRT) versus multifraction (MF-SBRT) regimens. **Methods:** A literature search was conducted across PubMed, Web of Science, Cochrane Library, Scopus, and Embase. Data analysis was performed using Engauge Digitizer, RevMan, and STATA software. **Results:** Fifteen studies were analyzed. SF-SBRT had a higher incidence of local failure but a lower rate of vertebral compression fractures (VCFs) compared to MF-SBRT. No significant differences were found in overall survival rates. The 1-year and 2-year local control rates for SBRT were 87% and 80%, with overall survival rates at 63% and 47%. **Conclusions:** SF-SBRT offers convenience and rapid relief, while MF-SBRT may provide better long-term control. Regimen selection should be based on the patient's clinical situation and preferences to optimize outcomes.

**Keywords** stereotactic body radiotherapy; spinal metastases; local control; overall survival; metaanalysis

**To Cite This Article** Wenwen JIANG, et al. (2024). Comparative Efficacy of Single-Fraction versus Multi-Fraction Stereotactic Body Radiotherapy for Spinal Metastases: A Meta-Analysis. *Medical Research*, 6(3), 103–118. https://doi.org/10.6913/mrhk.060310

*Medical Research*, ISSN 2664-0333 (print), ISSN 2664-0341 (online), DOI 10.6913/mrhk, a bimonthly, founded on 2018, Indexed by CNKI, Google Scholar, AIRITI, Scilit, CrossRef, Elsevier PlumX, etc., published by Creative Publishing Co., Limited. Email: wtocom@gmail.com, https://mrhk.cc, https://cpcl.hk.

## 1 Introduction

The vertebral column is the most common site for the metastasis of malignant neoplasms, with approximately 70% of all bone metastases occurring in the spine<sup>[1]</sup>. Patients with spinal metastases often present with low back pain or vertebral fractures as initial symptoms. As the metastases progress, they can lead to spinal cord compression, with metastatic epidural spinal cord compression (MESCC) occurring in about 8% to 20% of cases<sup>[2]</sup>.

Stereotactic body radiotherapy (SBRT), characterized by its non-coplanar, multi-angular, and focused irradiation techniques, represents a precision approach in oncological treatment<sup>[3]</sup>. This method involves accurate positioning, meticulous planning, and precise delivery of highly conformal, ablative radiation doses to the tumor while minimizing exposure to surrounding healthy tissue<sup>[4]</sup>. SBRT not only enhances local control, crucial for halting tumor progression, but also potentially reduces the risk of complications such as radiation-induced myelopathy or vertebral collapse<sup>[5,6]</sup>. Compared to conventional external beam radiotherapy (cEBRT), SBRT offers better protection of normal tissues and organs, superior pain relief, and improved control over local metastases<sup>[7]</sup>. Tumors such as melanoma, renal cell carcinoma, sarcoma, and those recurring after cEBRT remain particularly susceptible to the therapeutic effects of SBRT<sup>[8,9]</sup>.

The efficacy of radiotherapy is significantly influenced by the fractionation of radiation doses, which can be delivered in either single or multiple fractions. Despite the clinical importance of dose fractionation in spinal SBRT, there is considerable variation in the dose-fractionation schemes employed. Randomized controlled trials (RCTs) specifically investigating the optimal strategy for pain management, local tumor control, and side effects are notably lacking.

## 2 Methods

#### 2.1 Inclusion Criteria

The treatment must involve the use of stereotactic radiosurgery (SRS) or SBRT for patients diagnosed with spinal metastases, including those treated after decompression surgery or following the failure of conventional external beam radiotherapy (cEBRT). Publications must report at least one measurable outcome relevant to the study objectives. Studies authored by the same individual but reporting data from distinct institutions are eligible for inclusion.

#### 2.2 Exclusion Criteria

Studies focused on metastatic tumors located outside the spinal region, research involving primary spinal tumors, non-metastatic, or benign spinal conditions were excluded. Article types limited to reviews and case reports were also excluded, as well as publications with insufficient data to allow for the extraction of relevant outcomes. Non-English language publications were excluded as well.

#### 2.3 Descriptive Data

Comprehensive descriptive information was collected, including the author's name, year of publication, number of vertebral bodies affected by the tumor, patient cohort size, primary tumor histology, radiation dosage and fractionation scheme, duration of follow-up, prior decompression surgery, history of conventional external beam radiotherapy (cEBRT), and the type of publication. These details are systematically summarized in Table 1.

Author/ Year	Study Type	Lesions	Mean age(ran	Main Histology	Dose /SF	Dose /MF	Follow- up(Mon)	Prior RT	Prior Surgery
Bate 2015[ <b>35</b> ]	R	SF:38 MF:31	ge) 59.8 (29-81)	Renal(26%) Breast(24%) Lung(16%)	23/1 22/1 20/1 16/1	10/2 9/3 6/5	(range) 10	30 (43%)	21 (30%)
Bernstein 2016[ <b>36</b> ]	Р	SF:10 MF:17	58.4(33 .4-79.4)	Thyroid(100%)	18/1 16/1	30/5 27/3	28.9	8 (29%)	8 (29%)
Bishop 2015[ <b>37</b> ]	R	SF:146 MF:130	59 (17-88)	Renal(38%) Lung(14%) Thyroid(10%)	18/1 24/1	27/3	19	163 (49%)	NA
Cunha 2012 <b>[38]</b>	R	SF:36 MF:131	57 (18- 90)	Renal(29%) Breast(23%) Lung(20%)	20-22/1 8-18/1	18-24/2 20-27/3 30/4 23-35/5	7.4 (0.4-37.3)	54 (32%)	NA
Ghia 2016[ <b>39</b> ]	Р	SF:21 MF:26	62 (38–75)	Renal (100%)	24/1	27/3 30/5	23	NA	15 (32%)
Hashmi 2016[ <b>40</b> ]	R	SF:148 MF:99	62 (18–89)	Breast(29.1%) Lung(16.6%) Kidney(13.1%)	8–15.9/1 16–18/1 18–22/1	2–5/per FX 6–6.9/per FX 7–7.9/per FX 8–8.9/per FX 9–20/per FX	8.1 (0.1–52.6)	247 (100%)	113 (46%)
Ho 2016 <b>[41]</b>	Р	SF:14 MF:24	60 (22– 88)	Renal (26%) Breast(18%) Lung (8%)	24/1 18/1 16/1	27/3 30/5 20/5	69(9–145)	17 (45%)	16 (42%)
Isabelle 2015 <b>[42]</b>	R	SF:141 MF:46	60.20 (33- 87.67)	Renal (100%)	10-18/1 20-24/1	18-24/2 18-30/3 25-30/4 25-30/5	8.02(0.03- 75.99)	34 (18%)	0 (0%)
Isabelle 2016[ <b>43</b> ]	Р	SF:37 MF:63	NA	Renal(32%) Lung(30%) Breast(15%)	12-24/1	20-24/2 24-35/3-5	7.3(0.6-67.6)	23 (23%)	0 (0%)
Kumar 2017 <b>[44]</b>	R	SF:20 MF:10	65 (40- 89)	Thyroid (17%) Colon (13%) Breast (13%)	24/1	27-30/3-5	20 (5-40)	NA	NA
Laufer 2013 <b>[45]</b>	R	SF:40 MF:146	58.9 (14.8– 81.4)	Renal (22%) Sarcoma (18%) Prostate (13%)	24/1	30/5-6 27/3	11 (1.5-63.2)	91 (49%)	186 (100%)
Park 2014 <b>[46]</b>	R	SF:1 MF:58	NA	Breast(18.7%) Liver(13.6%) Stomach(11.9) Lung(11.9)	18/1	21-26/3-5 27/3; 27/5 28-30/3-5 32-35/5	7.4(1.1-42.5)	14 (23.7%)	NA
Randa 2016 <b>[47]</b>	Р	SF:18 MF:51	58 (20-80)	Renal(53%) Sarcoma(20%) Thyroid(9%)	16/1 18/1 20/1 24/1	30/5 27/3	30(1-145)	69 (100%)	31 (47%)
Sahgal 2013 <b>[48]</b>	R	SF:209 MF:201	57.55 (18-90)	Renal(55%) Breast(13%) Lung(10%)	8-17/1 18-26/1	18-26/2 18-35/3 25-35/4 25-35/5	11.5(0.03 - 113)	94 (23%)	NA
Folker 2014 <b>[49]</b>	R	SF:68 MF:52	54 (25-84)	Sarcomas (100%)	18-24/1	24-36/3-6	12.3 (1-80.7)	33 (28%)	12 (10%)

	Table1.	Baseline	Characteristics	of All	Included	Studies
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R:retrospective studies

P:prospective cohort studies

#### 2.4 Primary Outcomes

• Post-radiation vertebral compression fracture (VCF): Identified through imaging as either the emergence of a new vertebral body fracture or the exacerbation of an existing

fracture subsequent to SBRT.

- **Radiation failure:** Defined as imaging-documented progression of spinal tumors following SBRT, irrespective of the fractionation regimen employed.
- **Cumulative incidence of overall survival:** The probability of patient survival over time following SBRT.

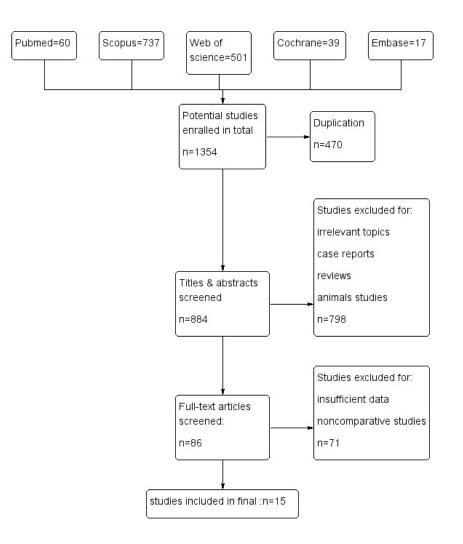


Figure 1: Flow diagram for the process of included studies identification

### 2.5 Secondary Outcomes

- Actuarial overall survival rate: Reported at both 1-year and 2-year intervals post-SBRT.
- Actuarial local control rate: Also reported at 1-year and 2-year intervals post-treatment.

## 2.6 Data Analysis

Statistical analyses were conducted using Review Manager (RevMan) and STATA version 13. Vertebral compression fractures (VCFs) and local failure were analyzed as dichotomous outcomes,

reported with odds ratios (ORs) and 95% confidence intervals (CIs). Time-to-event outcomes were expressed using hazard ratios (HRs). The choice between the random-effects model and the fixed-effects model was determined by the level of heterogeneity among the studies, with the random-effects model applied when heterogeneity was significant (I<sup>2</sup> > 50%) and the fixed-effects model used otherwise (I<sup>2</sup> < 50%). For studies lacking sufficient data, statistical transformations were performed, or indirect data were extracted using Engauge Digitizer software.

## 2.7 Quality Assessment

The quality of non-randomized controlled studies was evaluated using the Newcastle-Ottawa Scale (NOS), which employs a star system with a maximum of 9 stars to assess three critical aspects: the selection of study groups, the comparability of the groups, and the ascertainment of outcomes for cohort studies<sup>[15]</sup>. The processes of data extraction, analysis, and quality assessment were independently conducted by two unbiased clinicians. In cases of disagreement, a third party was consulted to resolve the issue.

# 3 Results

This study adheres to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the Methodological Quality of Systematic Reviews) guidelines<sup>[16]</sup>. Our initial search across five major databases yielded 1,354 articles. After removing 470 duplicates, 884 unique articles were retained for further review. A thorough screening of titles and abstracts led to the exclusion of 798 articles, which were deemed irrelevant due to their nature as reviews, case reports, or basic science experiments. Detailed full-text reviews of the remaining 86 articles resulted in the inclusion of 15 studies that met our predefined inclusion and exclusion criteria. This final cohort consisted of 10 retrospective studies and 5 prospective cohort studies; no randomized controlled trials (RCTs) were included.

## 3.1 Quality Assessment

Quality assessment was conducted using the Newcastle-Ottawa Scale (NOS), with articles scoring 7 or higher deemed high-quality. Among the 15 included studies, 9 received a score of 7 stars, 5 were awarded 8 stars, and 1 achieved the maximum score of 9 stars. Consequently, all included studies were classified as high-quality according to the NOS criteria (Table 2).

## 3.2 Main Outcomes

• Post-radiation Vertebral Compression Fracture (VCF): Analysis of 8 articles documenting 1,077 lesions revealed no heterogeneity ( $I^2 = 0\%$ ), supporting the use of the fixed-effects model. The results showed that multifraction (MF) treatments were significantly more likely to result in post-radiation vertebral compression fractures compared to single-fraction (SF) treatments (P  $\leq 0.001$ , OR = 1.82, 95% CI = 1.26 to 2.63) (Figure 2).

Study/Year	Study Type	Selection	Comparability	Exposure
Bate 2015[ <b>35</b> ]	R	***	\$	☆☆
Bernstein 2016[36]	Р	**	**	***
Bishop 2015[ <b>37</b> ]	R	***	**	☆☆
Cunha 2012 <b>[38]</b>	R	**	**	☆☆
Ghia 2016 <b>[39]</b>	Р	***	\$	☆☆
Hashmi 2016 <b>[40]</b>	R	***	**	**
Но 2016 <b>[41]</b>	Р	***	**	***
Isabelle 2015[42]	R	***	**	***
Isabelle 2016[43]	Р	***	☆	***
Kumar 2017[44]	R	***	**	**
Laufer 2013[45]	R	***	**	***
Park 2014[46]	R	***	\$	***
Randa 2016[ <b>47</b> ]	Р	**	**	***
Sahgal 2013[48]	R	***	☆☆	***
Folker 2014 <b>[49]</b>	R	***	☆☆	☆☆

Table2. Newcastle-Ottawa Scale Scores of All Included Studies.

R:retrospective studies P:prospective cohort studies

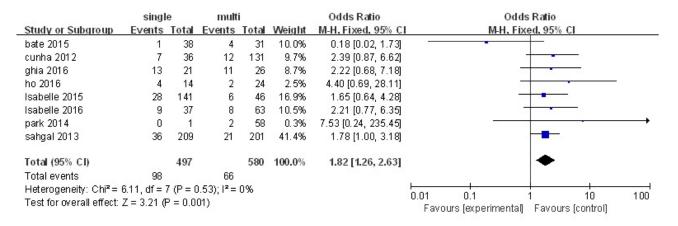


Figure 2: Comparison of Post-radiation Vertebral Compression Fracture in SF and MF Groups in the Meta-analysis

- Local Failure: An analysis of 7 articles covering 755 lesions demonstrated low heterogeneity ( $I^2 = 18\%$ ). Using the fixed-effects model, the findings indicated that SF treatments had a higher propensity for local failure compared to MF treatments (P = 0.0007, OR = 0.48, 95% CI = 0.31 to 0.73) (Figure 3).
- Cumulative Incidence of Overall Survival: The analysis of 4 articles encompassing 235 patients revealed no heterogeneity ( $I^2 = 0\%$ ), and thus the fixed-effects model was applied. The data indicated no significant difference in the cumulative incidence of overall survival between SF and MF treatments ( $P \ge 0.50$ , HR = 0.89, 95% CI = 0.63 to 1.25) (Figure 4).

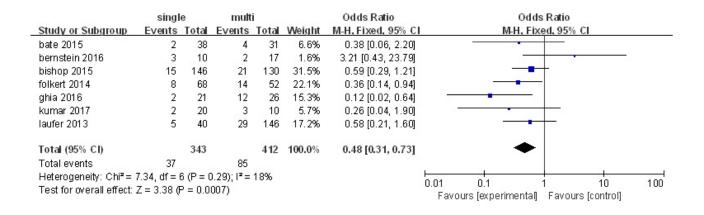


Figure 3: Comparison of Post-radiation Local Failure in SF and MF Groups in the Meta-analysis

Study or Subgroup	log[Hazard Ratio]	SE.	Weight	Hazard Ratio IV, Fixed, 95% Cl		Hazard Ratio IV. Fixed, 95%		
Study or Subgroup						IV, FIXed, 95%		
ho 2016	-0.47	0.5	11.9%	0.63 [0.23, 1.67]				
folkert 2014	-0.38	0.3	33.2%	0.68 [0.38, 1.23]		-		
Randa 2016	-0.0408	0.3328	27.0%	0.96 [0.50, 1.84]		-		
ghia 2016	0.27	0.327	27.9%	1.31 [0.69, 2.49]		· •		
Total (95% CI)			100.0%	0.89 [0.63, 1.25]		•		
Heterogeneity: Chi <sup>2</sup> = Test for overall effect:		); I <sup>2</sup> = 0%	)		0.01 0.1	1 single multi	10	100

Figure 4: Comparison of Post-radiation Cumulative Incidence of Overall Survival in SF and MF Groups in the Meta-analysis

#### 3.3 Secondary Outcomes

- One-Year Actuarial Local Control Rate: Analyzing data from 9 articles involving 1,037 lesions, we encountered low heterogeneity (I<sup>2</sup> = 24.8%), which supported the use of the fixed-effects model. The computed one-year actuarial local control rate was 87% (95% CI = 0.85 to 0.89) (Figure 5 A).
- Two-Year Actuarial Local Control Rate: Data from 7 articles covering 868 lesions also exhibited low heterogeneity (I<sup>2</sup> = 24.5%). Despite this, the random-effects model was employed, resulting in a two-year actuarial local control rate of 80% (95% CI = 0.78 to 0.83) following SBRT (Figure 5 B).
- One-Year Actuarial Overall Survival Rate: An assessment of 6 articles detailing the outcomes of 576 patients indicated moderate heterogeneity ( $I^2 = 66.0\%$ ), necessitating the use of the random-effects model. The calculated one-year actuarial overall survival rate post-SBRT was approximately 63% (95% CI = 0.55 to 0.70) (Figure 6 A).
- Two-Year Actuarial Overall Survival Rate: Analysis of 6 articles involving 544 patients revealed significant heterogeneity ( $I^2 = 72.7\%$ ), leading to the application of the random-

1-year actuarial tumor local control	ES (85% CI)	% Weight	B. 2-year actuarial tumor local control rate	ES (95% CI)
e (2015)	0.94 (0.89, 1.00)	13.24		
mstein (2016)	0.88 (0.76, 1.00)	2.68	bernstein (2016)	0.88 (0.76, 1.00)
shop (2015)	0.88 (0.85, 0.91)	32.95	bishop (2015)	0.83 (0.79, 0.87)
kert (2014)	0.88 (0.82, 0.94)	11.83	folkert (2014)	0.77 (0.70, 0.85)
ia (2016)	0.82 (0.71, 0.93)	3.34	ghia (2016)	0.68 (0.55, 0.81)
ishmi (2016)	• 0.83 (0.78, 0.88)	17.46	hashmi (2016)	0.78 (0.73, 0.83)
(2016)	0.85 (0.74, 0.96)	3.12	ho (2016)	0.82 (0.70, 0.94)
abelle (2016)	0.88 (0.81, 0.94)	9.72		
nda (2013)	0.85 (0.77, 0.93)	5.67	randa (2013)	0.79 (0.69, 0.89)
verall (I-squared = 24.8%, p = 0.223)	0.87 (0.85, 0.89)	100.00	Overall (i-squared = 24.5%, p = 0.242)	0.80 (0.78, 0.83)
	i			

Figure 5: Actuarial Local Control Rate following SBRT, as derived from the statistical analysis conducted in the included studies. 5A. One-Year Actuarial Local Control Rate. 5B. Two-Year Actuarial Local Control Rate.

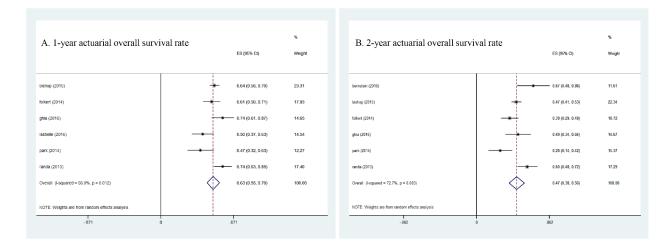


Figure 6: Actuarial Overall Survival Rate following SBRT, as derived from the statistical analysis conducted in the included studies. 6A. One-Year Actuarial Overall Survival Rate. 6B. Two-Year Actuarial Overall Survival Rate.

effects model. The two-year overall survival rate post-SBRT was determined to be around 47% (95% CI = 0.38 to 0.56) (Figure 6 B).

## 4 Conclusion

This study highlights the nuanced differences between single-fraction and multifraction SBRT in the management of spinal metastases. While both treatment regimens exhibit distinct biological effects, they do not significantly differ in terms of overall survival rates. Single-fraction SBRT offers advantages in treatment duration and cost-effectiveness, potentially improving patient compliance. However, the choice between single-fraction and multifraction SBRT should be individualized based on the patient's clinical context, taking into account the risk of vertebral compression fractures and the institution's capacity to manage potential complications. Despite the absence of randomized controlled trials in this area, our findings contribute valuable insights to the current understanding of SBRT fractionation. Future research should prioritize the inclusion of RCTs to further validate these observations and support evidence-based decision-making in the treatment of spinal metastases.

## 5 Discussion

#### 5.1 Comparative Efficacy of cEBRT and SBRT

Conventional external beam radiotherapy (cEBRT) remains a cornerstone of radiotherapeutic practice, typically delivering doses ranging from 1 to 4 Gy per fraction, with 1.8 to 2 Gy being the most common regimen. This approach allows for a broad range of radiation therapy targets to be treated at relatively low dose fractions<sup>[17]</sup>. A 2012 meta-analysis evaluating the comparative efficacy of different cEBRT fractionation patterns in treating bone metastases across various sites found that pain control rates were equivalent across the fractionation schedules<sup>[12]</sup>. However, spinal metastases present a unique challenge, requiring a dual-focused approach: precise control of the radiation dose for effective tumor targeting and stringent protection of adjacent normal tissues, particularly the spinal cord. In this complex therapeutic landscape, Stereotactic Body Radiotherapy (SBRT) offers distinct advantages. SBRT's capability for high precision and targeted radiation delivery makes it a superior modality for managing spinal metastases, enhancing treatment efficacy while minimizing risks to critical structures around the tumor site. This underscores the pivotal role of SBRT in contemporary management.

#### 5.2 Advantages of SBRT in Spinal Metastases

SBRT is renowned for its precision in delivering high radiation doses directly to the target volume while preserving the integrity of adjacent high-risk organs, especially the spinal cord. This advanced modality allows for an intense, focused dose ranging from 6 to 30 Gy, distributed across 1 to 5 fractions. These regimens leverage the differential radiobiological sensitivity of normal and tumor tissues, with an alpha/beta ( $\alpha/\beta$ ) ratio of 2 for the spinal cord to minimize risk and an  $\alpha/\beta$ ratio of 10 for tumor tissue to maximize therapeutic effect. This distinction underscores SBRT's capability to achieve significant tumor control while adhering to stringent safety margins for the protection of critical structures<sup>[18]</sup>.

### 5.3 Challenges in Dose Fractionation for SBRT

Despite its advantages, the optimal dose-fractionation schedule for spinal SBRT remains a topic of ongoing debate. Clinical practices vary widely, with single-fraction regimens delivering 16 24 Gy, alongside schedules of 24 27 Gy in 3 fractions, and 30 35 Gy over 4 5 fractions<sup>[19-21]</sup>.

Current evidence does not definitively favor one fractionation pattern over another in terms of efficacy. The incidence of vertebral compression fractures (VCFs) following spinal SBRT has been quantitatively assessed in two significant multicenter analyses, reporting VCF rates ranging from 6% to 14%. About half of these fractures were new occurrences post-SBRT, while the remainder involved pre-existing conditions that worsened following treatment. These observations suggest a nuanced balance between therapeutic efficacy and the risk of adverse effects such as VCF<sup>[22,23]</sup>.

#### 5.4 Vertebral Compression Fractures and Associated Risks

Tseng et al.<sup>[24]</sup> reported cumulative incidences of VCF following SBRT, documenting rates of 8.5% at 1 year and 13.8% at 2 years among 145 patients with 279 metastatic lesions. Their findings identified lytic tumors and spinal malalignment as significant predictors of VCF. In comparison, the SC.24 trial revealed a VCF rate of 11% in the SBRT-treated cohort, versus 17% in those receiving cEBRT, suggesting a differential impact of radiotherapy modality on the risk of VCF.

Vertebral compression fractures are a recognized complication following radiation therapy, primarily due to the high doses of radiation that can induce necrosis, cellular injury, vascular fibrosis, collagen degradation, and other biomechanical alterations. These changes collectively compromise bone integrity, weakening it and increasing susceptibility to fractures<sup>[25]</sup>. A 2007 meta-analysis highlighted variability in the incidence of VCFs after spinal SBRT, noting that these rates exceed the traditional baseline of around 3% seen with conventional radiotherapy<sup>[26]</sup>. The time between SBRT and the onset of VCFs varies, ranging from 2.5 to 25 months, with the highest risk occurring within the first 3 months.

#### 5.5 Clinical Outcomes and Local Control Rates

Multifraction SBRT leverages the differential capacity for DNA repair in normal versus tumor cells to mitigate radiation-induced damage. This approach narrows the therapeutic window between effective antitumor doses and the tolerance levels of critical adjacent structures, such as the spinal cord and esophagus. Consequently, it enables the delivery of higher total doses to the tumor while minimizing harm to surrounding healthy tissues, particularly beneficial for treating larger tumors or those close to vital organs, and in cases requiring retreatment<sup>[27]</sup>.

Compared to cEBRT, SBRT demonstrates superior local control, with tumor control rates ranging from 61% to 86% at one year<sup>[28]</sup>, and an average one-year survival rate of 76%<sup>[29]</sup>. For vertebral metastases from solid tumors, SBRT is recommended at doses exceeding an equivalent of 18 Gy in a single fraction (biologically effective dose, BED<sub>10</sub> = 50 Gy<sub>10</sub>). High-dose SBRT regimens for de novo spine metastases include 20 Gy in one fraction, 24 Gy in one fraction, 12 Gy in two fractions, 10 Gy in three fractions, and 7 Gy in five fractions. These schedules are associated with expected local control rates of 80% to 90% at one to two years<sup>[30,31]</sup>.

In a randomized phase III trial involving 117 oligometastatic patients, 56% of whom had spinal metastases, a comparison was made between single-fraction SBRT delivering 24 Gy and fractionated SBRT delivering 27 Gy in three fractions. The study found that the higher-dose, single-fraction SBRT resulted in improved local control<sup>[32]</sup>. Based on this study and supporting evidence, we recommend a dose exceeding the equivalent of 18 Gy in a single fraction (BED<sub>10</sub> = 50 Gy<sub>10</sub>) to achieve sustained local control in oligometastatic patients. However, higher doses increase the risk of VCFs, particularly with single-fraction regimens such as 24 Gy. The decision to use such a regimen depends on an institution's ability to manage potential complications, prompting some clinicians to opt for fractionated SBRT delivered over 2 5 fractions. In our analysis, the one-year local control rate was 87%, with a one-year survival rate of 63%, consistent with previous findings<sup>[33,34]</sup>.

## 5.6 Future Directions for SBRT Research

Our study reveals that the two SBRT fractionation patterns—single-fraction and multifraction exhibit distinct biological effects, yet do not significantly differ in terms of overall survival rates. From a patient perspective, single-fraction SBRT offers advantages in treatment duration and cost-effectiveness, potentially improving patient compliance compared to the multifraction approach. Despite the absence of randomized controlled trials (RCTs) as a reference, these findings provide valuable evidence to the existing literature. Future research should focus on integrating more RCTs to validate these observations and strengthen the evidence supporting SBRT fractionation choices.

Conflict of Interest: The authors declare that they have no conflict of interest.

**Data Availability Statements:** The data underlying this article will be shared on reasonable request to the corresponding author.

## Article History

Received: May 26, 2024 Accepted: June 15, 2024 Published: September 30, 2024 References

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