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# Posterior treatment of ankylosing spinal diseases with thoracolumbar fractures: a network meta-analysis

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## Abstract

**Objective** The implementation of diverse surgical techniques plays a crucial role in managing ankylosing spinal diseases (ASDs), serving as invaluable tools. Presently, posterior surgery stands out as the predominant approach owing to its familiarity with anatomical structures; however, it comprises various methodologies that require a thorough comprehension for their suitable application. Henceforth, we performed a network meta-analysis to assess and prioritize the efficacy and safety of surgical interventions for ASDs.

**Methods** The databases PubMed, EMBASE, Cochrane Library, and CNKI (China National Knowledge Infrastructure) were systematically searched for both randomized and non-randomized studies. No restrictions were placed on the initial time periods or languages of the searches. Patients with thoracolumbar fractures accompanied by ankylosing spondylitis and diffuse idiopathic skeletal hyperostosis were included in this study. RevMan 5.4 and Stata 14.2 software programs were utilized for assessing literature quality and conducting data analysis.

**Results** A total of 20 trials involving 1116 patients with ASDs were included, encompassing 4 posterior approaches. Network meta-analysis revealed that Percutaneous puncture demonstrated favorable outcomes in terms of surgical duration, intraoperative blood loss, postoperative bed rest time, and hospital stay. Both percutaneous internal fixation and 3D assisted fixation exhibited alternating advantages in postoperative functional recovery.

**Conclusions** Based on the available evidence, it is evident that percutaneous instrumentation offers clear advantages over other forms of instrumentation. However, the quality of some studies is suboptimal and further high-quality randomized controlled trials are necessary to provide additional verification.

**Keywords** Posterior treatment, Ankylosing spinal diseases, Thoracolumbar fractures, Network-analysis

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## Introduction

The most common manifestations of ankylosing spinal diseases (ASDs) include ankylosing spondylitis and diffuse idiopathic skeletal hyperostosis (DISH) [1]. The occurrence of osteoporosis and ankylosis of the spinal column is frequently observed in patients with ASDs [2]. Spinal fractures can occur even with minimal or no definite force applied to the patient [3]. Leading to instability and devastating neurologic injuries [4]. The cervical spine is a frequently fractured site; however, clinically, thoracolumbar fractures are more common than previously recorded [5]. Due to the distinctive clinical features of ASDs in combination with thoracolumbar fractures, the treatment approaches vary slightly from those employed for common spinal fractures. In recent years, surgery has emerged as the preferred treatment choice for the majority of patients [6].

The posterior pedicle screw internal fixation system is predominantly utilized for the treatment of adult spinal deformities (ASDs) in conjunction with thoracolumbar fractures [7]. The conventional surgical approach may induce significant patient trauma and give rise to numerous postoperative complications [8]. Due to the advanced pathological alterations of ankylosing spondylitis (AS), the accurate identification of normal anatomical landmarks proves to be challenging, especially with spinal kyphosis, which further increases the difficulty of pedicle screw placement [9]. This type of surgery is challenging, demanding a high level of expertise from the operator and repeated intraoperative fluoroscopy. Additionally, traditional surgical approaches may lead to soft tissue injury and affect the accuracy of screw placement, thereby prolonging the operation time, increasing intraoperative blood loss, and raising the incidence of postoperative complications [10].

In recent years, small incision surgery has gained wide acceptance in orthopedics as the concept of minimally invasive surgery has become prevalent, and its inherent advantages have undoubtedly been confirmed by a large number of experimental studies [11–13]. The field of orthopedics has rapidly incorporated digital medicine and 3D printing rapid prototyping manufacturing technology. By leveraging preoperative high-resolution CT scan data, it can accurately restore 3D bone morphology, replicate complex anatomical structures, and facilitate surgical planning and simulation [14–16]. The customized 3D printing guide template facilitates precise screw placement guidance during surgery and enables direct formation of the internal implant material [17–19].

Currently, posterior internal fixation techniques for thoracolumbar fractures in patients with ankylosing spondylitis encompass various methods, but the most optimal one remains undetermined. This study undertakes a network meta-analysis to compare and rank the efficacy of different posterior approaches for the first time, thereby providing valuable insights for clinical practice.

## Materials and methods

### Search strategy

The literature was reviewed by two investigators based on the principles of the patient/population intervention comparison outcome model. The keywords “fracture,” “ankylosing spondylitis,” and " diffuse idiopathic skeletal hyperostosis (DISH)” were searched in the titles and abstracts of articles in PubMed, EMBASE, The Cochrane Library, and CNKI (China National Knowledge Infrastructure). These terms were connected using the search operators “AND” and “OR”, The final search strategy was (fracture [Title/Abstract]) AND ((ankylosing spondylitis [Title/Abstract]) OR (diffuse idiopathic skeletal hyperostosis [Title/Abstract])). There were no restrictions on the initial time periods or languages of the searches; only articles published before January 1, 2024 were considered. Eligible articles were selected according to predetermined criteria. In cases of disagreement, more experienced individuals made final decisions regarding article selection.

### Selection criteria

**(1)** Participants: The inclusion criteria for this study were ankylosing spondylitis and DISH diagnosed by certain criteria, fracture confirmed by CT or MRI, posterior long-segment fixation after consent, no age limit; the exclusion criteria were severe concomitant diseases, multiple concurrent fractures, other spinal diseases, allergies or psychological disorders, and cases with conservative or external fixation treatment.

**(2)**Intervention and comparison: The study exclusively focuses on posterior internal fixation surgery, excluding patients who have undergone alternative surgical procedures.

**(3)**Outcomes: The operation time, intraoperative blood loss, postoperative bed rest time and hospital stay were evaluated as the main outcomes. Complications, screw placement accuracy, VAS score, JOA score, cobb Angle of injured segment and MacNab score at 6 months after operation were evaluated as the general outcomes. These indicators are not completely included in one article, and we select the results under the same conditions as required in each study.

**(4)**Study design: Randomized controlled trials and retrospective study considered qualified.

### Quality assessment

We utilized the Cochrane Handbook to assess the risk of data from randomized controlled trials, and based on the findings, we categorized the studies into three levels.

Additionally, for retrospective studies, we employed the Newcastle-Ottawa Scale (NOS) to evaluate article quality. Studies with NOS scores exceeding 5 were considered indicative of moderate to high-quality research. Any discrepancies were resolved through discussion or by the third researcher.

### Data extraction

Two researchers independently screened each trial by reviewing titles, abstracts, and full text using standardized and piloted forms. The baseline information was extracted, including the first author, publication date, country of origin, study design, sample size, mean age, sex distribution percentage, disease type, duration of follow-up examination (in months), and interventions. Discrepancies were resolved through discussion or by the third researcher.

### Data analysis and statistical methods

We utilized Review Manager, version 5.3 and STATA14.2 for data analysis. The risk ratio (OR) and its corresponding 95% confidence interval (CI) were employed to calculate the dichotomous outcomes. Continuous variables were assessed using mean difference (MD) along with a 95% confidence interval. In cases where study heterogeneity was minimal, we applied the fixed effect model for network meta-analysis; otherwise, the random effect model was used. Global inconsistencies, loop inconsistencies, and local inconsistencies were estimated through 'network meta i', 'ifplot', and 'node-splitting' procedures respectively. Surface under the cumulative ranking curve (SUCRA) results were computed and a ranking chart was generated using Stata software to determine the relative superiority of dressing types.

## Results

### Search results

A total of 2906 articles were identified through our query method, with 802 originating from PubMed, 1118 from Embase, 78 from the Cochrane Library, and 908 from CNKI. Among these articles, a total of 483 studies were excluded due to duplication checking. Based on the relevance of their titles and abstracts, investigators selected a total of 2385 articles for further analysis. Ultimately, after thoroughly reading and comprehending the full text content, we included a final set of 20 articles in our study. The entire process of document screening is illustrated in Fig. 1.

### Risk of bias assessment

In these incorporated documents, the methodological quality of two types of experiments were evaluated according to their respective evaluation criteria which were mentioned in the methods and materials. Among the included studies, except six are RCTs, the rest are retrospective studies. Three RCTs are due to uncertainty and are not considered better quality. The bias is mainly in the selection bias. The retrospective studies were considered as good quality, the detail contents were exhibited in Fig. 2.

### Study characteristics

Of the twenty articles included, six were randomized controlled trials (RCTs), while fourteen were retrospective studies, all of which were conducted in single-center settings. Nearly every article provided comprehensive demographic information about the study population. Lastly, our study will encompass a total of 1116 individuals, with 543 patients undergoing traditional fixation, 366 patients opting for percutaneous fixation, 191 patients utilizing 3D printing assistance, and 16 patients receiving robot-assisted internal fixation. The pertinent details regarding these publications will be presented in Table 1.

### Outcomes of meta-analysis

#### *Primary outcomes-Operative time*

The network diagram depicted in Fig. 3A illustrates the eligible comparisons for operative time, with nodes representing the weighted number of trials for each comparison and edges reflecting the precision of direct estimates. SUCRA probabilities were utilized to compare and rank the effects of medical treatments on operative time. Notably, percutaneous fixation demonstrated superior effectiveness and achieved the highest Constant-Murley score (percutaneous:94.5%, 3D-printing:69.3%, robot-assisted:30.0%, traditional:6.2%. Figure 4A). Pairwise comparisons revealed that percutaneous fixation resulted in significantly shorter operative time compared to traditional, 3D-printing, and robot-assisted fixation (Fig. 5A). No significant publication bias was observed regarding the Constant-Murley score (Fig. S5A).

#### *Primary outcomes-Blood volume*

The network of eligible comparisons for blood volume is illustrated in Fig. 3B. The SUCRA probabilities indicate that percutaneous (SUCRA: 100.0%) and 3D-printing (SUCRA: 62.6%) exhibit relatively superior effects on blood volume compared to robot-assisted (23.8%) and traditional therapies (13.6%), as shown in Fig. 4B. Pairwise comparisons presented in Fig. 5B demonstrate that percutaneous therapy is associated with lower blood volume than other treatment options. No significant publication bias was observed regarding blood volume, as depicted in Supplementary Figure S5B.

#### *Primary outcomes-Bed rest time*

The network of eligible comparisons for bed rest time is illustrated in Fig. 3C. It should be noted that the

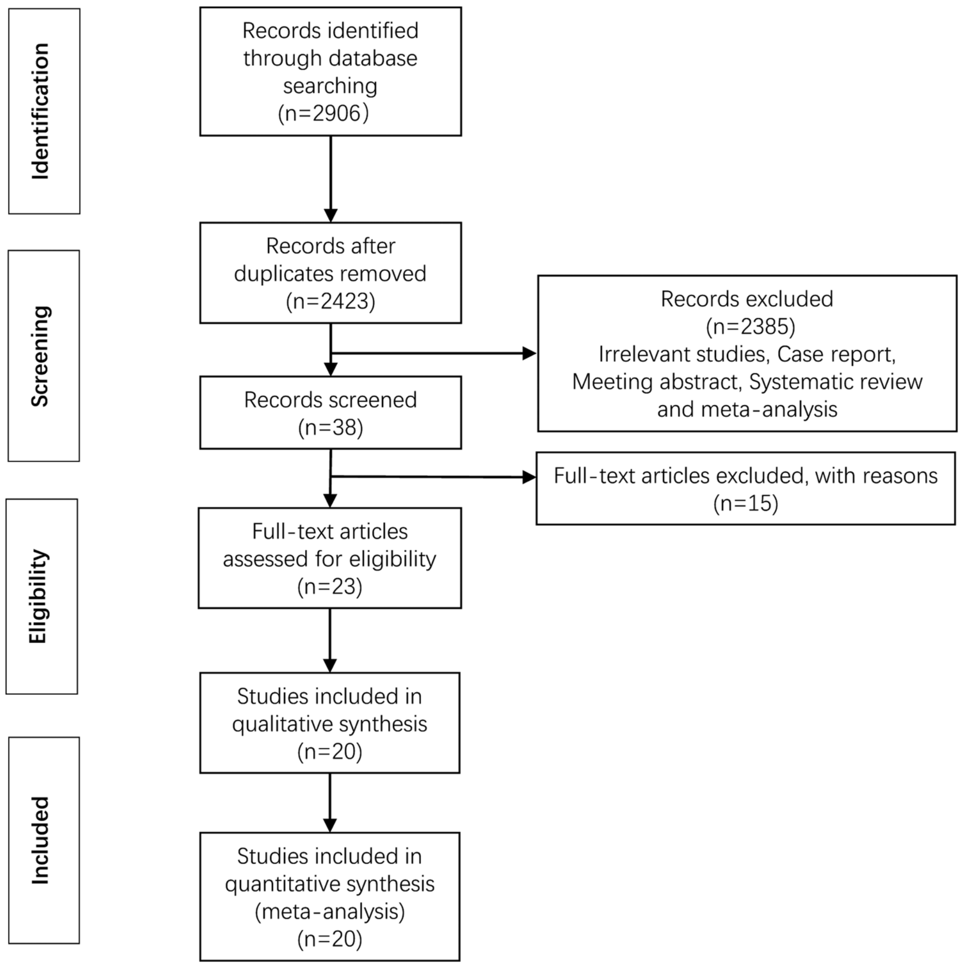



**Fig. 1** Flowchart of the study selection process

utilization of percutaneous fixation (SUCRA: 89.8%) and robot-assisted fixation (SUCRA: 51.4%) demonstrated relatively superior efficacy compared to traditional fixation (SUCRA: 8.8%) (Fig. 4C). The pairwise comparison results for bed rest time are presented in Fig. 5C, revealing significant differences between percutaneous and traditional fixation methods. No substantial publication bias was observed regarding EQ-5D outcomes (Figure S5C).

#### *Primary outcomes-Hospitalization duration*

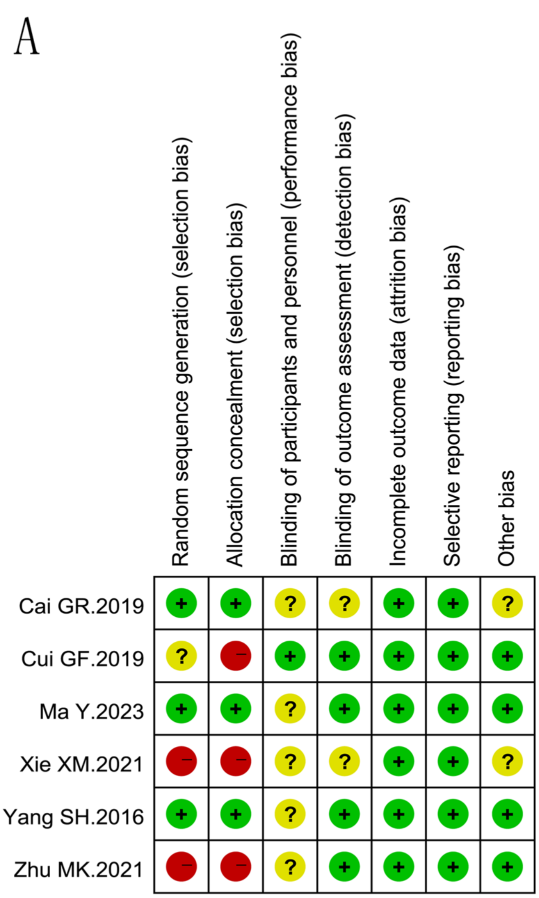
The network diagram in Fig. 3D illustrates the eligible comparisons for hospitalization duration. According to the SUCRA probabilities, percutaneous therapy (SUCRA: 97.1%) demonstrates relatively superior effects on hospitalization duration compared to robot-assisted (SUCRA: 34.6%) and traditional approaches (18.2%), as shown in Fig. 4D. The pairwise comparison results depicted in Fig. 5D indicate that percutaneous therapy is associated with a shorter length of hospital stay when compared to open surgery. No significant publication bias was observed regarding the risk of secondary surgery, as illustrated in Figure S5D.

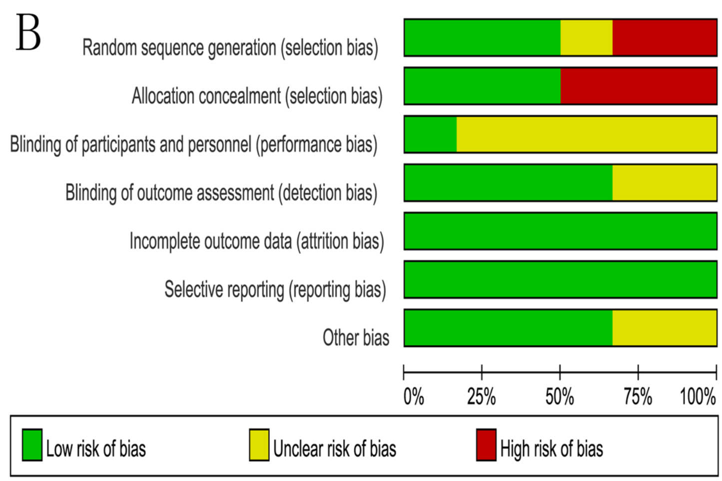
### Secondary outcomes-Complication

The network of eligible comparisons for the complication is illustrated in Fig. 3E. The SUCRA probabilities indicate that 3D printing therapy (SUCRA: 78.9%), percutaneous therapy (SUCRA: 60.0%), robot-assisted therapy (SUCRA: 51.2%), and traditional therapy (SUCRA: 9.9%) exhibit varying degrees of effectiveness on the complication. With the exception of traditional fixation, all other therapies demonstrate relatively superior outcomes for managing complications (Fig. 4E). Pair-wise comparison results for the complication are presented in Fig. 5E, revealing a higher incidence of complications associated with traditional open surgical treatment. No significant publication bias was observed regarding the risk of secondary surgery (Figure S5E).

#### *Secondary outcomes-The accuracy of screw*

The network of eligible comparisons illustrating the accuracy of screw is depicted in Fig. 3F. It should be noted that the utilization of 3D printing (SUCRA: 15.9%) and robot-assisted techniques (SUCRA: 25.0%) exhibited relatively superior efficacy in percutaneous therapy (SUCRA:

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| Study | Selection | Comparability | Outcome |
|---|---|---|---|
| Lindtner RA 2017.4 | *** | ** | *** |
| Okada E, N 2019.5 | ** | ** | ** |
| Jiang P 2019.4 | ** | ** | *** |
| Chung WH 2020.3 | * | ** | ** |
| Yang CB 2020.4 | ** | * | *** |
| Li XQ 2021.10 | ** | ** | *** |
| Liang K 2021.2 | ** | ** | *** |
| Ye JY 2022.11 | ** | ** | *** |

**Fig. 2** Risk of bias assessment of RCT studies. (**A**) Risk of bias graph. (**B**) Risk of bias summary; Quality assessment score of the retrospective study(**C**)

59.8%) compared to traditional methods (SUCRA: 99.4%), as shown in Fig. 4F. The pairwise comparison results depicted in Fig. 5F demonstrate significant differences in screw accuracy between 3D printing and traditional fixation methods. No evidence of publication bias was observed for EQ-5D (Figure S5F).

### *Secondary outcomes-Other clinical index*

The details of other indices, including the VAS score, JOA score, and cobb angle of the injury segment in the sixth month, as well as the MacNab score, will be provided. The network diagrams illustrating eligible comparisons are presented in Fig.S1. In terms of JOA score, patients treated with percutaneous interventions (SUCRA: 77.3) exhibited superior outcomes compared to those receiving traditional approaches (SUCRA: 68.8) and 3D printing techniques (SUCRA: 3.9). The utilization of 3D printing demonstrates superior efficacy in restoring the physiological curvature of the spine for the cobb angle of injury segment in the sixth month (3D printing: SUCRA: 99.9, percutaneous: SUCRA: 37.7, traditional: SUCRA: 12.4). The percutaneous fixation method demonstrates significant efficacy in providing pain relief for patients (percutaneous: SUCRA: 71.2, 3D printing: SUCRA: 61.4, traditional: SUCRA: 17.4). Additionally, in terms of MacNab outcomes, patients treated with 3D printing exhibited the highest performance (3D printing: SUCRA: 82.9, percutaneous: SUCRA: 63.9, traditional: SUCRA: 3.2). These results are illustrated in Figure S2. The pairwise comparison results are presented in Figure S3. No significant evidence of publication bias was observed for these findings (Figure S4).

## Discussion

The percutaneous surgery outperformed 3D printing surgery, robot-assisted surgery, and traditional open surgery in terms of operative time, operative bleeding, postoperative bed rest time, and length of hospital stay. The term "robot-assisted technology" refers to the utilization of robots in assisting with screw placement during traditional surgical procedures [20]. In terms of screw placement accuracy, 3D printing is the best method, with no significant difference between conventional and robot-assisted treatments, but it significantly outperforms others, partly due to suboptimal X-ray imaging and the obliteration of anatomical structures in osteoporosis

**Table 1** Summary of characteristics in the studies included

| Author/year | Country | Study design | No.patients | Age(Y) | Male | Disease type | Follow-up examination(M) | Interventions |
|---|---|---|---|---|---|---|---|---|
| Yang SH.2016 | China | RCT | 12/11 | Nr | Nr | AS | 6 | Traditional/ 3D + printing |
| Wang YH.2017 | China | Retro | 43/43 | 41.5/44.3 | 24/26 | AS | 12 | Traditional/ 3D + printing |
| Cai GR.2019 | China | RCT | 25/25 | 44.5/44.3 | 16/15 | AS | 6 | Traditional/Percutaneous |
| Cui GF.2019 | China | RCT | 45/47 | 42/41 | 25/26 | AS | 6 | Traditional/ 3D + printing |
| Jiang P.2019 | China | Retro | 20/21 | 52/65 | 12/13 | AS | 28.4 ± 2.3 | Traditional/Percutaneous |
| Yan CB.2020 | China | Retro | 19/20 | 39.5/38.5 | 13/15 | AS | 6 | Traditional/Percutaneous |
| Li XQ.2021 | China | Retro | 50/70 | 60.20/60.45 | 32/44 | AS | 6 | Traditional/Percutaneous |
| Liang K.2021 | China | Retro | 65/54 | 53.23/52.66 | 34/30 | AS | 12 | Traditional/Percutaneous |
| Xie XM.2021 | China | RCT | 41/41 | 52.33/53.10 | 25/23 | AS | 6 | Traditional/Percutaneous |
| Zhu MK.2021 | China | RCT | 45/46 | 41.63/42.35 | 31/30 | AS | 3 | Traditional/ 3D + printing |
| Shi YF.2022 | China | Retro | 18/8 | 62.22/66.25 | 18/4 | AS | 3 | Traditional/ Robot + assisted |
| Lin S.2023 | China | Retro | 7/8 | Nr | Nr | AS | 11.2 ± 1.1 | Traditional/ Robot + assisted |
| Ma Y.2023 | China | RCT | 36/36 | 51.26/51.81 | 24/25 | AS | 3 | Traditional/ 3D + printing |
| Shen SB.2023 | China | Retro | 7/8 | 56.29/54.75 | 4/5 | AS | 12–20 | Traditional/ 3D + printing |
| Lindtner RA.2017 | Austria | Retro | 14/6 | 76.4/70.6 | 12/6 | AS/Dish | 29.2 | Traditional/Percutaneous |
| Okada E, N.2019 | Japan | Retro | 25/16 | 77.9/76.1 | 18/12 | Dish | 12 | Traditional/Percutaneous |
| Chung WH.2020 | Malaysia | Retro | 7/14 | 69.3/69.1 | 6/9 | AS/Dish | 35.3 ± 27.8 | Traditional/Percutaneous |
| Ye JY.2022 | China | Retro | 21/26 | 55.43/58.12 | 15/21 | AS | 33.81 | Traditional/Percutaneous |
| Felix C. Kohler.2022 | Germany | Retro | 27/48 | 72/77 | 19/33 | AS/Dish | Nr | Traditional/Percutaneous |
| Moussallem.2016 | USA | Retro | 16/25 | 75.25/75.76 | 16/19 | AS/Dish | Nr | Traditional/Percutaneous |

Traditional: Traditional fixation, Percutaneous: Percutaneous fixation, 3D + printing:3D printing assisted fixation, Robot + assisted: robot-assisted internal fixation, RCT: randomized controlled trial, Retro: retrospective study, AS: Ankylosing spondylitis, Dish: diffuse idiopathic skeletal hyperostosis, Nr: Not reported, D: Day, M: Month, Y: Year, No.:number

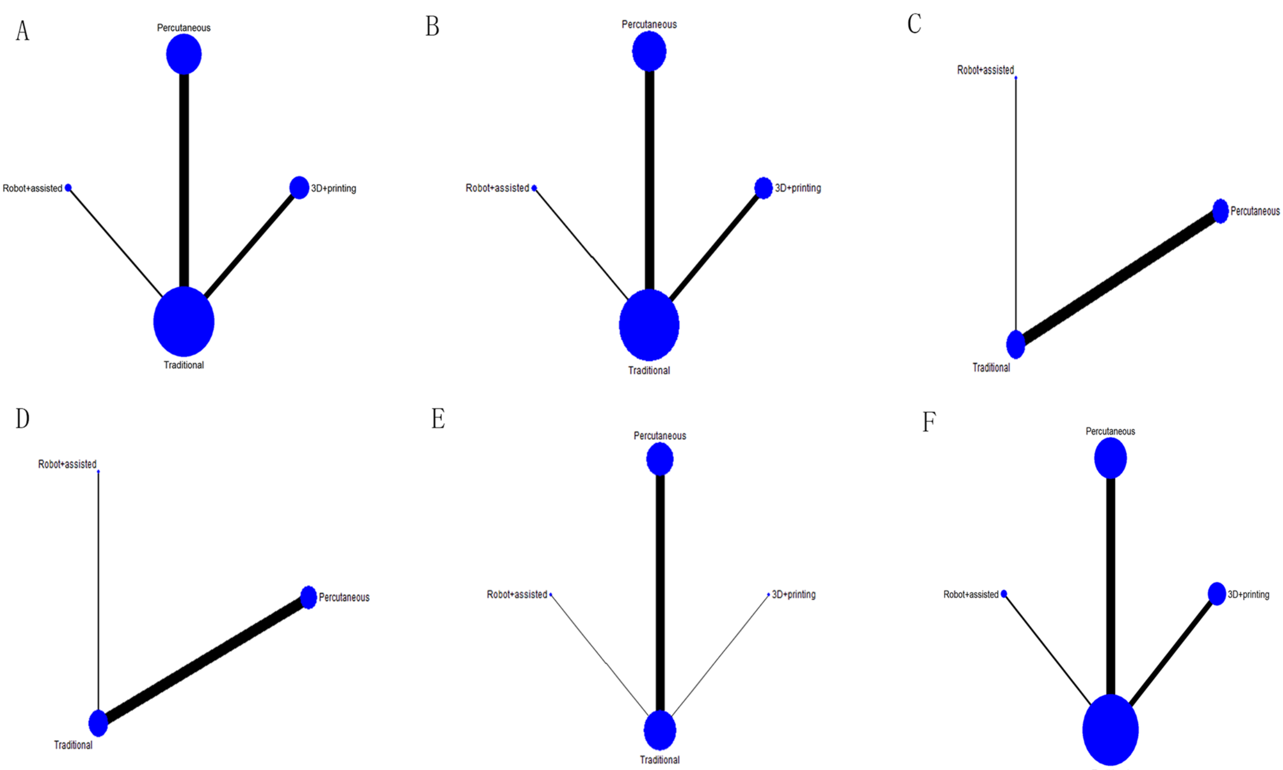


**Fig. 3** Network of comparisons for the operative time (**A**), blood volume (**B**), bed rest time (**C**), hospitalization duration (**D**), complication (**E**) and the accuracy of screw (**F**) included in the analysis. Traditional: Traditional fixation, Percutaneous: Percutaneous fixation, 3D-printing:3D printing assisted fixation

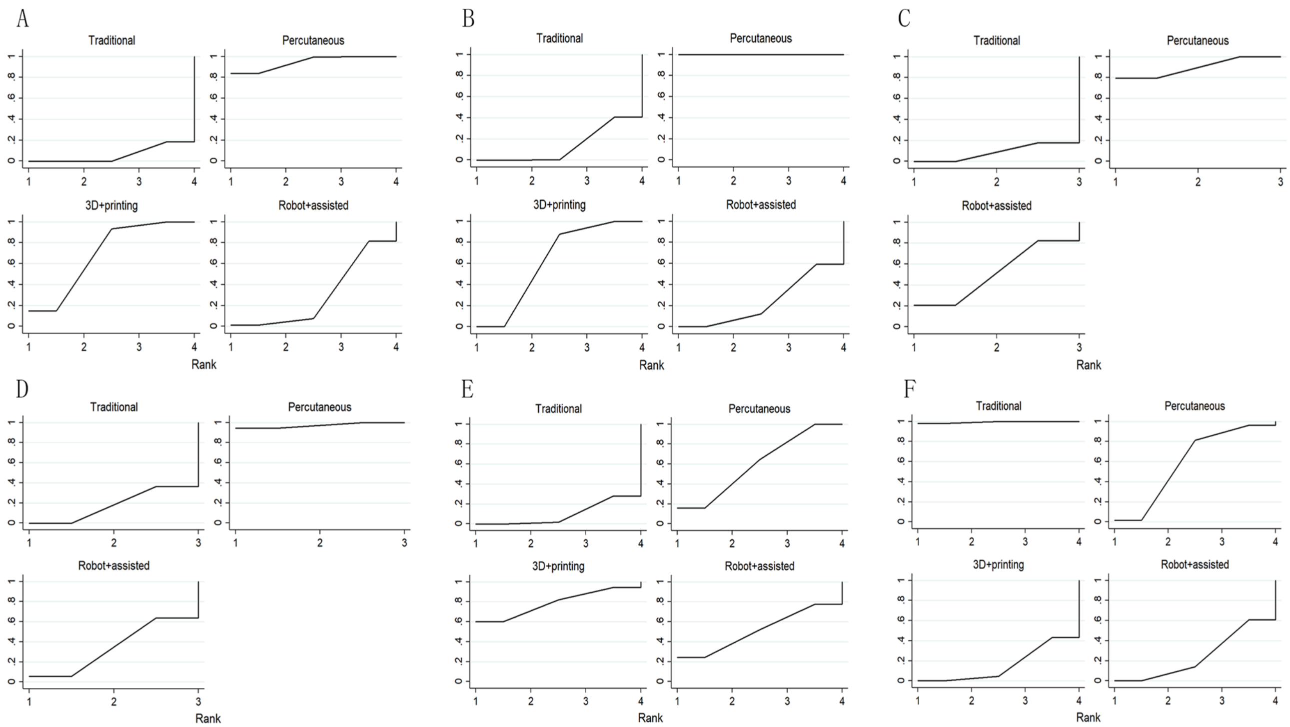


**Fig. 4** The SUCRA (surface under the cumulative ranking) probabilities for the operative time (**A**), blood volume (**B**), bed rest time (**C**), hospitalization duration (**D**), complication (**E**) and the accuracy of screw (**F**) included in the analysis. Traditional: Traditional fixation, Percutaneous: Percutaneous fixation, 3D-printing:3D printing assisted fixation

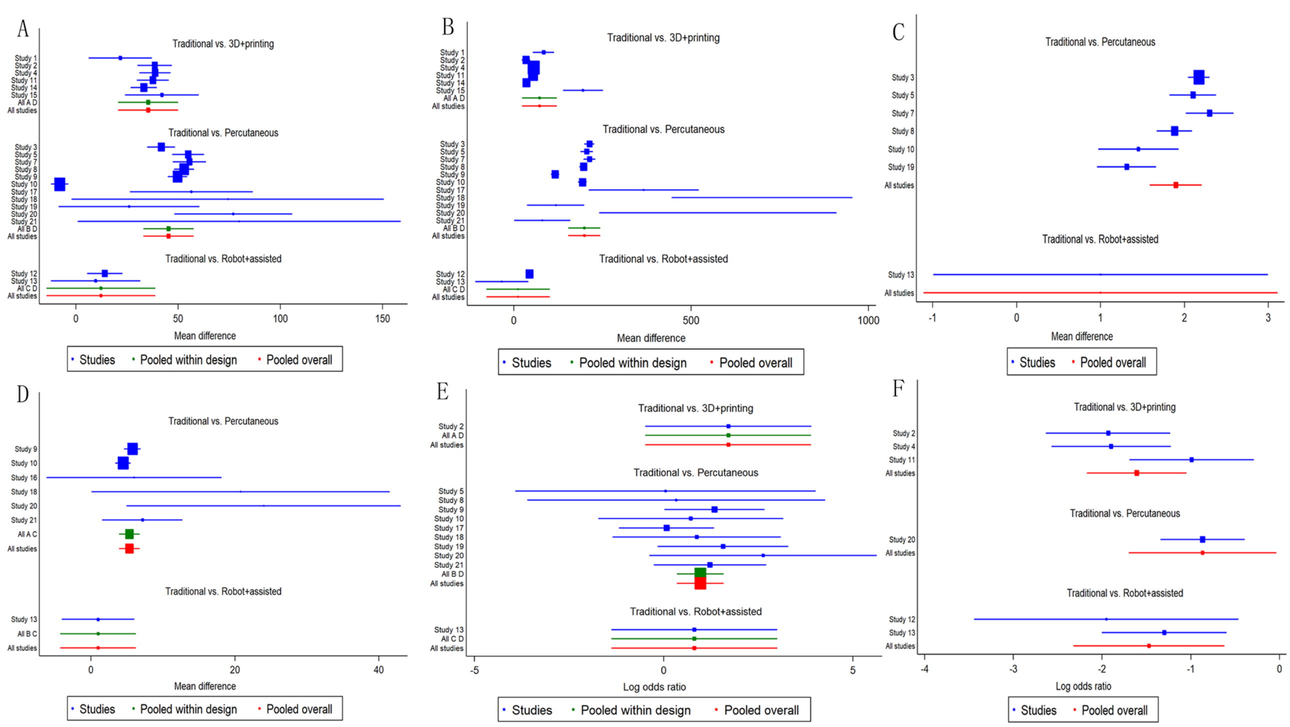


**Fig. 5** Pair-wise comparisons of treatments for the operative time (**A**), blood volume (**B**), bed rest time (**C**), hospitalization duration (**D**), complication (**E**) and the accuracy of screw (**F**) included in the analysis. Traditional: Traditional fixation, Percutaneous: Percutaneous fixation, 3D-printing:3D printing assisted fixation

patients [21]. The advantage of 3D over robotic assistance in terms of operation time and intraoperative blood loss lies in the pre-completion of 3D printed models and designs prior to surgery, whereas robot assistance necessitates performance during surgery. The aforementioned circumstances will consequently result in the prolongation of operative duration, leading to an escalation in surgical hemorrhage, augmented patient trauma and associated surgical risks, compromised patient functionality, extended bed rest and hospitalization periods, as well as excessive utilization of medical resources. Therefore, percutaneous surgery aligns with the concept of minimally invasive procedures and effectively mitigates harm inflicted upon patients [22, 23].

The incidence of postoperative complications in ASD patients undergoing spinal fracture surgery is high, with pulmonary complications, urinary tract issues, incision infections, deep vein thrombosis (DVT), anemia, and loose internal fixation being the most common [24–27]. Urinary tract infections and deep vein thrombosis (DVT) were found to be associated with postoperative status and early mobilization. These associations were primarily attributed to the duration of surgery and length of hospital stay, thereby confirming the elevated incidence of complications in the traditional open surgery group [28, 29]. The occurrence of incision infection and anemia is associated with the length of the surgical incision and the extent of trauma. "Multiple keyhole" incisions and percutaneous pedicle screw insertion, which involve minimal muscle dissection, result in reduced bleeding rates, shorter hemostasis and wound closure time, as well as decreased operation duration, thereby leading to a lower incidence of hemorrhagic shock [30–32].

The issue of implant loosening during posterior spinal instrumentation surgery is a significant concern in these patients, with reported rates of loosening as high as 15% [33]. The issue of osteoporosis aside, the occurrence of internal fixation loosening is also associated with repetitive nail path adjustments [34]. Raditional surgery relies heavily on the surgeon's expertise and repeated intraoperative fluoroscopy, particularly in obese patients, which can increase surgical complexity and necessitate multiple nail movements. The use of a cannulated screw system has been suggested as an optional solution for nail loosening, while injecting an appropriate amount of bone cement to enhance the implant's grip strength. However, it should be noted that this approach may carry a potential risk of cement leakage. The avoidance of strenuous activity is still recommended, particularly in elderly patients, to minimize the risk of screw loosening and refracture [35]. The cortical bone trajectory screws can also enhance the retention force of pedicle screws within the cancellous bone pathway, particularly for preventing screw pullout in osteoporotic bone [36–38].

The application of robot-assisted technology is predicated on the availability of costly equipment and introduces heightened intricacy to surgical procedures. With the advancement of 3D printing technology, it not only assumes a role in preoperative operations but also facilitates screw placement during surgeries. The application of the 3D printing guide plate in correcting severe kyphosis secondary to AS proved pivotal during the surgical procedure, significantly contributing to postoperative functional recovery of patients [39]. The 3D printing guide template was subsequently utilized in thoracolumbar spine surgery. The findings demonstrated a significant enhancement in the precision of thoracolumbar pedicle screw placement through the implementation of 3D printing technology [40, 41]. The placement of screws by hand necessitates the removal of solidified tissue and osteophytes from the vertebral body, resulting in prolonged surgical duration, increased intraoperative blood loss, and heightened risk of postoperative complications such as peripheral nerve injury. The utilization of 3D printing guide plate enables a direct fit to the vertebral body, thereby minimizing tissue damage, enhancing surgical safety, and improving overall surgical success rates. The utilization of this technology can effectively decrease the frequency of X-ray exposure during surgery for both patients and surgeons, thereby reducing iatrogenic injuries to a certain extent. In comparison with navigation and robot-assisted screw placement techniques, 3D printing significantly minimizes material and equipment costs while being applicable in general hospital settings.

The present network meta-analysis, being the first of its kind on the utilization of Posterior treatment internal fixation in patients with ASDs, although limited by a small sample size, will yield more robust evidence for clinical practice. Some limitations of this study need to be considered. The number of included studies was too small, and given the insufficient data for some outcome measures, we could not identify a high degree of homogeneity by subgroup analysis, which requires a large number of studies with good sample sizes to provide more definitive conclusions.

## Conclusion

Based on the analysis of existing evidence, percutaneous internal fixation and 3D-assisted fixation demonstrated alternating advantages in terms of VAS score, MacNab score, cobb angle of the injured segment, and JOA score. Percutaneous puncture exhibited favorable outcomes in operation time, intraoperative blood loss, postoperative bed time, and hospital stay. We should master the advantages of various kinds of surgery, according to the patient's condition personalized choice of treatment plan, at the same time should explore the shortcomings of various surgical methods, observe whether can be further improved, and carry out data collection. Therefore, further large-scale sample studies with multi-center participation and high-quality methodologies are required to validate these findings.

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12891-025-08700-1.

Supplementary Material 1

Supplementary Material 2

### Author contributions

Search articles- Bo Yang, Chaochao Zhang, Wei Guo; Data analysis-Fujiang Cao, Fangfang Wang; Manuscript preparation-Jiaxiao Shi; Manuscript revision-all authors.

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### Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethical approval

Not applicable.

### Consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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