Study on the efficacy and safety of the Shi's cervical rotational manipulation for patient with atlantoaxial joint subluxation: study protocol for a randomized controlled trial.

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Abstract

Background? The clinical diagnosis of atlantoaxial joint subluxation (AJS) in Traditional Chinese Medicine (TCM) is characterized by an unequal distance between the lateral mass of the atlas and the odontoid process on imaging, resulting in neck pain accompanied by symptoms such as dizziness, headache, and limited cervical mobility. In Shanghai, Shi's cervical rotational manipulation (SCRM) is a commonly employed TCM manual therapy for the treatment of this condition. Nevertheless, there is a lack of evidence-based medical research regarding the clinical efficacy and safety assessment of this technique. Therefore, the principal objective of this study is to evaluate the efficacy and safety of SCRM in patients diagnosed with AJS.
Methods/design: This study is a prospective, randomized controlled clinical trial conducted at a single center, with a follow-up period of 24 weeks. A total of 96 patients diagnosed with AJS were recruited from outpatient and inpatient clinics at Shanghai Baoshan Hospital of Integrated Traditional Chinese and Western Medicine. These patients were randomly assigned to either the experimental group (SCRM) or the comparison group (basic cervical manipulation, BCM). Treatment sessions consisting of SCRM or BCM will be administered twice a week for a duration of 4 weeks. The participants will undergo treatment sessions with SCRM or BCM twice a week for a duration of 4 weeks. Clinical monitoring indicators encompass the presence or absence of clinical symptoms as recorded on a symptom recording form, cervical imaging examination using cervical CT, the degree of neck pain measured by the Visual Analog Scale (VAS), cervical range of motion assessed through cervical mobility measurement, the degree of vertigo evaluated using the Vertigo Symptoms Scale-Chinese Version (VSS-C), and any adverse events that may occur during the entire follow-up period. The time points for data collection and follow-up occurred at baseline and after the intervention, specifically during the 4th, 8th, 12th, 16th, 20th and 24th week.
Discussion: This paper presents an overview of the reasoning and structure of a prospective, randomized controlled trial with the objective of investigating the clinical efficacy and safety of SCRM in patients with AJS by assessing improvements in clinical symptoms, severity of neck pain, severity of vertigo, and changes in cervical imaging. If this study proves successful, it will offer trustworthy evidence regarding the efficacy and safety of SCRM for patients with AJS.
Trial registration: China Registered Clinical Trial Registration Center ChiCTR2300068510. Registration on 21 February 2023.

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Study on the efficacy and safety of the Shi's cervical rotational manipulation for patient with atlantoaxial joint subluxation: study protocol for a randomized controlled trial.

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Abstract

Background The clinical diagnosis of atlantoaxial joint subluxation (AJS) in Traditional Chinese Medicine (TCM) is characterized by an unequal distance between the lateral mass of the atlas and the odontoid process on imaging, resulting in neck pain accompanied by symptoms such as dizziness, headache, and limited cervical mobility. In Shanghai, Shi's cervical rotational manipulation (SCRM) is a commonly employed TCM manual therapy for the treatment of this condition. Nevertheless, there is a lack of evidence-based medical research regarding the clinical efficacy and safety assessment of this technique. Therefore, the principal objective of this study is to evaluate the efficacy and safety of SCRM in patients diagnosed with AJS.

Methods/design: This study is a prospective, randomized controlled clinical trial conducted at a single center, with a follow-up period of 24 weeks. A total of 96 patients diagnosed with AJS were recruited from outpatient and inpatient clinics at Shanghai Baoshan Hospital of Integrated Traditional Chinese and Western Medicine. These patients were randomly assigned to either the experimental group (SCRM) or the comparison group (basic cervical manipulation, BCM). Treatment sessions consisting of SCRM or BCM will be administered twice a week for a duration of 4 weeks. The participants will undergo treatment sessions with SCRM or BCM twice a week for a duration of 4 weeks. Clinical monitoring indicators encompass the presence or absence of clinical symptoms as recorded on a symptom recording form, cervical imaging examination using cervical CT, the degree of neck pain measured by the Visual Analog Scale (VAS), cervical range of motion assessed through cervical mobility measurement, the degree of vertigo evaluated using the Vertigo Symptoms Scale-Chinese Version (VSS-C), and any adverse events that may occur during the entire follow-up period.

The time points for data collection and follow-up occurred at baseline and after the intervention, specifically during the 4th, 8th, 12th, 16th, 20th and 24th week.

Discussion: This paper presents an overview of the reasoning and structure of a prospective, randomized controlled trial with the objective of investigating the clinical efficacy and safety of SCRM in patients with AJS by assessing improvements in clinical symptoms, severity of neck pain, severity of vertigo, and changes in cervical imaging. If this study proves successful, it will offer trustworthy evidence regarding the efficacy and safety of SCRM for patients with AJS.

Trial registration: China Registered Clinical Trial Registration Center ChiCTR2300068510. Registration on 21 February 2023.

Keywords: Atlantoaxial joint subluxation; Shi’s cervical rotational manipulation (SCRM); Efficacy and safety; Randomized controlled trial

Background

Joint subluxation is a distinct medical diagnosis within the realm of Traditional Chinese Medicine (TCM) [1]. In November 2020, the National Health Commission of China and the China Administration of Traditional Chinese Medicine officially incorporated the term "Joint Subluxation" into the updated edition of the "International Classification of Diseases 11th Revision, ICD-11" instead of "Gu Cuo Feng" which was previously widely used in TCM clinical diagnosis, thereby establishing its recognition as a universally accepted diagnostic term [2]. While joint subluxation can manifest in various articulations throughout the body, the spinal region, particularly the cervical spine, frequently serves as a prevalent site of occurrence [3]. Hence, in Traditional Chinese Medicine (TCM) diagnosis, the specific location of manifestation is referred to as the Joint Subluxation of the site, with the atlantoaxial joint subluxation (AJS) being a prevalent clinical condition. Meanwhile, AJS is also considered as a type of cervical spondylosis. The primary visual indication of AJS is the asymmetrical gap observed between the lateral mass of the atlantoaxial joint and the odontoid process on cervical spine X-ray or CT scans, and/or along with the misalignment of the axis spinous process relative to the midline of the spinous process [4].

The atlantoaxial joint, situated in the human cervical spine, functions as a relatively autonomous unit. Within this joint, the atlas assumes the role of the central axis for neck motion, contributing to over 40% of the rotational movement of the cervical spine. Conversely, the axis serves as the focal point for stress in the upper cervical spine and functions as a primary attachment site for the neck's short muscles and ligaments [5]. In instances where the atlantoaxial joint experiences a pathological state known as "Joint Subluxation," it can lead to the entrapment of the synovial membrane and joint capsule, resulting in localized swelling and pain in the cervical spine, impaired joint movement, and stimulation of the corresponding regions of the nerves, blood vessels, and receptors, which will cause symptoms such as vertigo and pain [6]. For a long time, the AJS has been commonly referred to as atlantoaxial joint instability, atlantoaxial joint disorder and so on [7, 8]. The clinical manifestations are mainly neck pain accompanied by dizziness, headache, and cervical limited mobility, so clinicians used to diagnose the patients as cervical vertigo [9, 10].

Cervical manipulation is a frequently employed approach in the management of cervical spondylosis, with cervical rotation manipulation or small joint mobilization being the most prominent technique [11, 12]. This method involves the rotation of the subject's head along the longitudinal axis of the cervical spine, resulting in an audible "clicking" sound from the cervical vertebra joint. The clinical utilization of this technique has garnered significant attention and has been supported by empirical evidence demonstrating its efficacy and safety through various studies. Studies have demonstrated

that this particular technique has the potential to ameliorate Joint Subluxation's pathological condition, restoring bones and joints to their typical physiological and anatomical alignments, and reestablishing dynamic and static mechanical equilibrium in the cervical vertebra joints, thereby accomplishing therapeutic objectives [13-15]. Nevertheless, variations in clinical effectiveness arise due to divergent approaches to manipulation, as well as the manipulation's focus on the atlantoaxial joint, a crucial anatomical region within the cervical spine, the safety of manual therapy has always been a concern of clinicians [16, 17].

Shi’s cervical rotational manipulation (SCRM) is the characteristic technique in treating AJS created by Shi’s traumatology TCM academic school which is the biggest traumatology school of TCM in Shanghai. The technical attributes of SCRM encompass the swift application of stress, which belongs to the high velocity and low amplitude (HVLA) technique. In our prior investigation, we formulated a standardized operating procedure (SOP) for SMT, which will be expounded upon subsequently [18]. Our research team quantified objective metrics, as well as kinematic and kinetic parameters, pertaining to the technique, considering the viewpoints of both recipients and practitioners [19]. Furthermore, we assessed the safety of the technique through a biomechanical lens and provided preliminary insights into its biomechanical mechanism of action [20]. In the clinical assessment of immediate efficacy for SCRM, a reduction of 50% in VAS scores was observed immediately following the procedure. Additionally, approximately 70% to 80% of participants reported subjective improvements such as a sensation of lighter heads, relaxed necks, or brighter eyes [18]. These findings suggest a significant immediate efficacy of the SCRM technique. In our subsequent short-term and medium-term clinical follow-up study, the intervention resulted in an efficacy rate of 94.74%. Furthermore, the overall efficacy rate at 3 months was 89.47%, with no notable discomfort or adverse events reported [18]. Nonetheless, there is still a lack of standard, randomized controlled studies on SCRM, which cannot provide evidence-based medical evidence for the efficacy and safety of SCRM. Consequently, the aim of this RCT was to assess the efficacy and safety of SCRM for patients with AJS.

Method/design

Study design

This study will be a single-center, prospective, randomized controlled clinical trial to evaluate the effectiveness and safety of SCRM for patients with AJS. We used the SPIRIT reporting guidelines to introduce this protocol [21]. A total of 93 subjects with AJS form outpatient and inpatient clinics will be recruited and randomly allocated to either the SCRM group or the BCM group. Screening (Visit 0) is undertaken within 3 days prior to enrollment to assess eligibility and collect baseline data as

well as their imaging data. Those participants who meet the inclusion criteria will be randomly assigned into the SCRM group or BCM group and receive the corresponding treatment of each group twice a week for 4 weeks. After the end of treatment (Visit 1), all patients will undergo evaluations and records including symptoms and signs, cervical mobility examination and measurement, VAS scores, VSS-C scores, imaging, efficacy evaluation and adverse events. Then all patients will be followed up every 4 weeks until the end of study at 24 weeks. Additionally, imaging and efficacy evaluation will be conducted at week 4 (Visit 1) and week 24 (Visit 6), VSS-C evaluation will be conducted at week 4 (Visit 1), week 16 (Visit 4) and week 24 (Visit 6). The flowchart schedule is shown in Table 1. and the flow diagram of participants is shown in Fig.1.

The Shanghai Baoshan Hospital of Integrated Traditional Chinese and Western Medicine will be responsible for recruiting, screening, and intervention of all subjects and assessment of all outcomes. Management of the randomization sequence and data analyses will be carried out by the Institute of Traumatology, Shi's Center of Orthopedics and Traumatology, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine. Ethics approval has been received from Shanghai Baoshan hospital of Integrated Traditional Chinese and Western Medicine. Informed written consent will be obtained from all participants.

Participants

Patients aged between 18-70 years with AJS will be included in the study. Inclusion criteria require patients to exhibit typical cervical imaging characteristics of the asymmetrical gap between the lateral mass of the atlantoaxial joint and the odontoid process on cervical spine X-ray or CT scans, and/or along with the misalignment of the axis spinous process relative to the midline of the spinous process. The screening, inclusion and exclusion procedures for all patients, as well as the notification and signing of informed consent, and the documentation of each follow-up visit, will be meticulously recorded by the participants on an individual basis.

Diagnostic criteria

The diagnosis of AJS is based on the Diagnostic Criteria for Traditional Chinese Medicine and the International Classification of Diseases 11th Revision (ICD-11), including the following aspects: (1) Have a history of neck strain or injury, and have a long-term habit of working and/or living with a low head. (2) The clinical manifestations are mainly vertigo, dizziness, headache or soreness in the neck. (3) The cervical movement is mainly limited to the left-right rotation of the atlantoaxial joint. When performing palpation, it can be found that the muscle tension around the atlantoaxial joint increases or small blocky or strip-shaped muscle nodules are felt, which may induce or exacerbate dizziness or vertigo. (4) Cervical X-ray or CT shows the asymmetrical gap observed between the

lateral mass of the atlantoaxial joint and the odontoid process, with a difference of more than 2mm, and/or along with the misalignment of the axis spinous process relative to the midline of the spinous process.

Inclusion criteria

(1) Met the diagnostic criteria of AJS. (2) Male or female 18 to 70 years old. (3) Recurrent clinical symptoms such as neck pain, vertigo, dizziness, and headache for less than 4 weeks and cannot be relieved. (5) Voluntarily participated in this trial and signed the informed consent document.

Exclusion criteria

(1) Has cervical spondylosis of nerve root type or spinal cord type and severe spinal stenosis. (2) Has a history of spinal surgery or severe spinal trauma. (3) Has a history of congenital variation or malformation of unstable cervical vertebral structure. (4) Dizziness or vertigo caused by other diseases diagnosed by specialized examinations such as cardiovascular, otolaryngology, and neurology departments. (5) Imaging findings include spinal infection, fracture, tumor, tuberculosis, severe spinal deformity, severe osteoporosis, ankylosing spondylitis, and osteitis deformans. (6) Combined with severe primary diseases of endocrine system, cardiovascular system, autoimmune system, tumor or mental illness. (7) Pregnant or recently pregnant women, as well as breastfeeding women. (8) Those who cannot accept cervical manipulation therapy.

Withdrawal criteria

(1) The subjects who have severe or intolerable adverse reactions during the observation process. (2) The subjects who have persistent or progressive symptoms and are not suitable for participating in the trial. (3) The subjects who may be at risk of health damage (such as sudden serious complications. (4) The subjects who voluntarily withdrew or missed the interview due to other reasons.

Sample size

The sample size calculation was based on our previous clinical research in cervical spondylosis of nerve root type patients using the same primary outcome instrument. The efficiency of CSM is 89.5%, while that of BCM is 54.6%. The sample size calculation formula: $n_1=n_2=\frac{1}{2}\left(\frac{u_\alpha+u_\beta}{\sin^{-1}\sqrt{P_1}-\sin^{-1}\sqrt{P_2}}\right)^2$ with α of 0.05, 1-β of 0.90. According to estimations, 48 participants per group were needed considering this is a long-term follow-up that is expected to dropout at a rate of no greater than 20%. **Randomization and allocation**

The randomization schedule will be prepared by the Institute of Traumatology, Shi's Center of Orthopedics and Traumatology, Shuguang Hospital Affiliated to Shanghai University of Traditional

Chinese Medicine. The specific randomization number lists will be computer-generated using IBM SPSS 22.0 (version 22.0, IBM, Corp., New York, NY, USA) and concealed from the screeners, assessors and patients by a specialized staff who is not involved in the study. It is stipulated that within a set of randomly generated numbers, odd numbers are attributed to the SCRM group, while even numbers are attributed to the BCM group. Subsequently, all numbers and their respective group assignments are documented on a card and securely sealed within opaque envelopes. These envelopes are then labeled with sequential numbers corresponding to the patients and entrusted to the screeners, who bear the responsibility of participant screening. Once a patient has been successfully enrolled, provided written informed consent, completed the baseline measurements, and is confirmed as an eligible participant, the sealed envelope will be transferred to the manual therapist. The manual therapist will unseal the envelope and administer the intervention (SCRM or BCM) based on the instructions provided on the card. The allocation list, containing sensitive information, will be kept confidential by specialized personnel who are not involved in participant recruitment or outcome assessment. This information will not be disclosed to the data analysts or outcome assessors.

Blinding

Participants will be unaware of their group assignment and will remain unaware of whether they received SCRM or BCM treatment. The outcome assessors will also be unaware of the randomization allocation and will not be involved in the intervention process. The manual therapists will not be able to be blinded due to their involvement in performing the interventional protocols. However, they will not participate in the outcome measurements or statistical analyses, and will be instructed to refrain from disclosing treatment details to the outcome assessors or participants. The statistician will remain blinded to the group allocation until the completion of the statistical analyses.

Interventions

The techniques used in this study are SCRM in the experimental group and BCM in the control group. The two techniques are commonly used in clinical treatment and have established SOP in Shanghai. All patients will receive treatment twice a week, with a 2-day interval between sessions, for a duration of 4 weeks. In addition, there is a relaxation therapy step before the two techniques after which the SCRM or BCM operation will be performed. The relaxation therapy step will be performed as follows:

1 The patient assumes a seated position, while the manipulation therapist positions themselves behind one side of the patient's body.

2 One hand of the therapist provides support to the patient's forehead, while the other hand employs pressing, pulling, and kneading techniques on both sides of the patient's cervical

spine, as well as the trapezius, sternocleidomastoid, and levator scapulae muscles, repeating these actions three times.

3 Subsequently, the therapist applies pushing techniques along the line extending from the seventh cervical spine to the acromion, repeating this action three times.

Note: The entirety of the relaxation therapy session lasts approximately 10 minutes.

Shi's cervical rotational manipulation (SCRM)

The primary technological approach in SCRM involves applying pressure with the thumb on the spinous process, transverse process, or pedicle of the patient's axis, while simultaneously rotating the cervical spine in an effort to restore it to its original alignment. AJS is categorized into eight distinct techniques, which are determined by the specific imaging characteristics of the atlantoaxial joint (Fig. 2 shows the comprehensive classification of AJS under X-ray). Each technique within these categories employs different SCRM methods.:

(1) *Simple asymmetrical gap between the lateral mass of the atlantoaxial joint and the odontoid process type:* Specifically, the spinous process of the axis remains aligned with the midline of the spinous process, yet the discrepancy in distance between the lateral mass of the left and right atlas and the dentate process is evident. Should the left block exhibit a 2mm greater distance compared to the right block, it falls under Type A (left oblique type). Conversely, if the right block displays a 2mm greater distance than the left block, it is classified as Type B (right oblique type).

(2) *Simple misalignment of the axis spinous process relative to the midline of the spinous process type:* The distance between the lateral masses of the left and right atlas and the dentate process is either equal or exhibits a difference within a 2mm range. However, the spinous process of the axis deviates from the midline of the spinal axis. If the spinous process of the axis is positioned to the left of the midline, it is classified as Type C (left rotation type). Conversely, if the spinous process of the axis is located to the right of the midline, it is categorized as Type D (right rotation type).

(3) *Mixed type:* If Type A merges with Type C, it is Type AC. If Type A merges with Type D, it is Type AD. If Type B merges with Type C, it is Type BC. If Type B merges with Type D, it is Type BD.

The SOP of SCRM according to different types are as follows [18]:

Type A:

(1) The patient assumes a seated position, while the medical therapist stands behind the patient's left side. The therapist's left hand supports the patient's forehead, specifically positioning the right thumb at the left transverse process of the patient's axis. The remaining four fingers of the therapist's right hand rest gently on the right side of the patient's neck, resulting in a forward

flexion of the patient's neck by approximately 10°.

(2) The therapist subsequently alters the position of their left hand, placing it on the patient's right chin nodule, while maintaining the unchanged posture of the right hand. This adjustment allows the therapist to rotate the patient's neck to its maximum range of active movement.

(3) The therapist's left hand persists in applying force to achieve the maximum range of passive movement in rotating the patient's neck, while the right thumb maintains a fixed position. The patient is instructed to relax their neck. Subsequently, the left hand momentarily intensifies the force of left rotation, while the right thumb applies pressure to the transverse process in a rightward direction. This maneuver often elicits an audible "click" sound emanating from the neck, accompanied by a subtle sliding sensation beneath the therapist's right thumb. And, the procedure is considered concluded.

Type B

(1) The therapist stands behind the patient’s right side, the therapist’s right hand supports the patient's forehead, specifically positioning the left thumb at the right transverse process of the patient’s axis.

(2) The remaining steps are the same as *Type A*, except that they are all in the opposite direction.

Type C

The operation steps are the same as *Type A*, while the right thumb of the therapist is fixed at the left spinous process of the patient’s axis.

Type D

The operation steps are the same as *Type B*, while the left thumb of the therapist is fixed at the right spinous process of the patient’s axis.

Type AC

The operation steps are the same as *Type A*, while the right thumb of the therapist is fixed at the left pedicle of the patient’s axis.

Type AD

(1) The first operation steps are the same as *Type A.*

(2) The second operation steps are the same as *Type D.*

Type BC

The operation steps are the same as *Type B*, while the left thumb of the therapist is fixed at the right pedicle of the patient’s axis.

Type BD

(1) The first operation steps are the same as *Type B.*

(2) The second operation steps are the same as *Type D.*

Basic cervical manipulation (BCM)

The operation of BCM does not differ depending on the type of AJS. All types of AJS patients will undergo the following SOP [18]:

(1) The patient assumes a seated position, the manipulation therapist stands behind the patient's left side.

(2) The therapist manipulates the patient's jaw by flexing their left elbow and applies pressure to the occipital area with their right hand, which is holding the household registration and supporting the other four fingers.

(3) Subsequently, the therapist gradually rotates the patient's head to the left until reaching the active limit position, and then instructs the patient to relax their neck while the therapist continues to rotate the head to the passive limit position using both hands. During this process, a momentary force is exerted to further facilitate the left rotation of the patient's head, resulting in audible clicking sounds emanating from the neck.

(4) Then, the therapist will perform the steps (1)-(3) above again on the right side of the patient.

Note: There is no requirement for the implementation sequence on the left and right sides.

Follow-up period

The follow-up assessments with questionnaires will be conducted. During the 24-week unsupervised follow-up period, no participants will undergo special therapy with the exception of routine cervical care.

It is important to acknowledge that every subsequent patient will schedule an appointment in advance via telephone and visit the outpatient department. Subsequently, the outcome assessors will aid patients in completing the questionnaire, conduct and document physical examinations, and administer cervical CT scans.

The outcome assessors will establish an electronic information group, inviting all participants to join. Throughout the follow-up period, any adverse events or physical discomfort experienced in any circumstance can be promptly reported within the information group.

Outcome measurement

The following baseline descriptive data will be obtained by questionnaire: age, gender, marital status, education level, occupation, and basic medical history and drug combination. A summary of all measures and following-up time point in this trail is shown in Table 1.

Primary outcome

Efficacy Rate (ER)

The clinical symptoms of all subjects will be recorded and evaluated by Numerical rating scale (NRS) which was composed by a horizontal line with a length of 0-10 cm, and the anchor words are “0” for “normal” and “10” for “unbearable”. Referring to the efficacy evaluation standards in the "Diagnostic and Therapeutic Efficacy Standards for Traditional Chinese Medicine Diseases" issued by the China Administration of Traditional Chinese Medicine in 1994.

We define Clinical Cured (CC) as: The NRS score for clinical symptoms has decreased by more than 80%, and patients can live and work normally.

We define Clinical Improvement (CI) as: The reduction in NRS scores for clinical symptoms ranges from 20% to 80%.

We define Clinical Cureless (CCs) as: The NRS score for clinical symptoms is reduced by less than 20%.

We define Clinical Recurrence (CR) as: The original symptoms reappear after treatment and the degree is equivalent to or aggravated before treatment.

All patients will be followed up and the ER will be calculated at Visit 1 after the intervention. The ER and CR rate will be calculated at Visit 6. The calculation formula is as follows:

ER= (Numbers of CC + Numbers of CI – Numbers of CCs)/ Total numbers of patients 100%

CR rate = Numbers of CCs/ (Numbers of CC + Numbers of CI) 100%

Secondary outcomes

The severity of neck pain (VAS)

The VAS score is used to evaluate the severity of neck pain of all subjects [22]. The VAS score sheet consists of a horizontal 100mm long line segment with "painless" and "extremely painful" ends. Patients select a point on the line segment based on their own pain perception and draw a vertical line through that point to express the intensity of pain.

The severity of vertigo (VSS-C)

The VSS-C scale has been used in many studies to evaluate the severity of vertigo and has shown high reliability and validity [23]. The VSS-C is a self-assessment scale consists 22 questions with a score of 0-4 for each question. A total score of 0-33 points indicates mild vertigo; A score of 34-67 indicates moderate vertigo; A score of 68-101 indicates severe vertigo; A score of 102-136 indicates extremely severe vertigo.

Imaging changes of cervical CT

All participants will undergo cervical CT examination at Visit 0, Visit 1 and Visit 6. Two radiologists will measure the distance from the lateral mass of the atlantoaxial joint to the dentate process and the distance from the axis to the midline of the spinous process. Each radiologist will measure each

image three times and the average of the six outcomes will be taken as the final result. Then, the improvement rate will be calculated based on the results. The calculation formula is as follows:

Improvement rate = (Distance of pre-treatment – Distance of after treatment)/ Distance of pre-treatment 100%

Cervical mobility

A cervical inclinometer instrument will be used to measure the cervical mobility. The outcome assessor will measure and record the angles of the patient's cervical in six directions: flexion, extension, left rotation, right rotation, left lateral bending and right lateral bending [24]. The outcome assessor will take 3 measurements in each direction, and take the average of the 3 values as the final result.

Adverse events

Any adverse events, including symptoms, signs and physical or laboratory examination abnormalities, will be carefully evaluated and recorded. Researchers will analyze the causes of these AE, make judgments, and track and record them in a timely manner. Once an AE occurs, doctors will provide the corresponding treatment to the patient for free. All AE must be judged for their character, severity, and potential relationship to the study treatment. The correlation between AE and study treatment is divide into five levels: definitely related, probably related, possibly related, possibly unrelated, and definitely unrelated. Based on the judgment and severity of AE, the primary investigator and ethics committee will be reported immediately to decide whether to discontinue observation, retain medical records of subjects who withdrew from the experiment, conduct a full dataset analysis of their efficacy and adverse reactions, and fill in the experiment conclusion and the reason for case withdrawal.

Data collection and management

An electronic information data collection system for our research has been created by the Institute of Traumatology, Shi's Center of Orthopedics and Traumatology. All data collection will be electronic, double-checked and backed up by two research assistants and entered into the system for mutual verification and correction of errors. Once all electronic data is verified against the original data, the data will be locked, and any modification and their reasons will leave a trace in the data backend.

Statistical analysis

The main objective of this study is to evaluate the clinical effectiveness of SCRM therapy in patients with AJS. Additionally, secondary analyses will be conducted to assess changes in VAS, VSS-C, imaging findings, and cervical mobility before and after treatment in AJS patients. Analyses will be performed using IBM SPSS 22.0 (version 22.0, IBM, Corp., New York, NY, USA). The

measurement data will be expressed using mean differences (mean ± standard deviation). The repeated measurement data will be analyzed using within-group variance analysis. Enumeration data will be presented as rates. The sample size needed for the Pearson chi-square test, comparing rates between the two groups before and after treatment, will be determined using the normal approximation algorithm and a one-sided test. This study employs the superiority test, utilizing a one-sided test level α=0.05. In the event that $P \leq 0.05$, it signifies the rejection of H0, thereby establishing the superiority of the SCRM group over the BCM group. Conversely, if P 0.05, it indicates that a definitive conclusion regarding superiority cannot be drawn at this stage. The safety analysis will employ the chi-square test to compare the incidence of adverse reactions between the two groups. In instances where the data fails to meet the requirements of the chi-square test, the *Fisher's* exact probability method will be employed.

Discussing

Globally speaking, manual therapy is considered one of the most crucial clinical therapies for the treatment of cervical spondylosis, such as spinal manipulation, chiropractic, Mulligan's technique, small joint adjustment technique and HVLA technique are widely used [25-27]. In the context of China, doctors employ diverse techniques in the treatment of various regions and schools, each possessing distinct technical attributes. In Shanghai, China, the most prevalent technique employed is SCRM, which has demonstrated satisfactory therapeutic outcomes [28]. However, there exists a dearth of evidence-based medical evidence regarding its efficacy and safety. Consequently, this study aims to examine the effectiveness and safety of SCRM in treating patients with AJS through a prospective, randomized controlled trial.

The optimal sample size has been accurately determined based on the findings of our prior research to guarantee sufficient test performance [18]. Subsequently, randomization and blinding procedures have been fully implemented to ensure the study's classification as a randomized controlled trial. Additionally, a statistical analysis employing a superiority test has been conducted to ascertain that all patients with AJS can receive authentic clinical treatment. As Shi’s orthopedics and traumatology academic school with manual therapy is well known throughout China, with a history of 160 years, and it is officially recognized by Chin’s health care administration and Shanghai Baoshan Hospital is also a branch of Shi’s orthopedics and traumatology academic school, and we ensure the interventions (SCRM or BCM) will be performed by a fixed chief physician with a more then 10 years of clinical experience. Moreover, proficient research assistants have been assigned to carry out the screening, selection, and follow-up stages, possessing a comprehensive understanding of the research process for all subjects. These measures will greatly contribute to enhancing patients'

adherence and mitigating the likelihood of attrition in this study. In terms of evaluation metrics, we will employ appropriate standards and develop meticulous professional scales as the primary outcome evaluation indicators to prevent subjective and ambiguous classification assessments, thereby minimizing data distortion and bias. Additionally, we have developed a dedicated electronic information data collection system for this study, guaranteeing the precision, novelty, and security of the data.

In brief, this study aims to examine the clinical effectiveness and safety of SCRM in patients with AJS by assessing improvements in clinical symptoms, severity of neck pain, severity of vertigo, and changes in cervical imaging. If successful, this investigation will yield dependable evidence regarding the efficacy and safety of SCRM for individuals with AJS.

Trial status

This trial was registered at ClinicalTrials.gov on 21 February 2023 (identifier ChiCTR2300068510). Recruitment was stated in March 2023.The last follow-up data is predicted to be collected by the end of February 2025.

Abbreviations

AJS: atlantoaxial joint subluxation; TCM: Traditional Chinses Medicine; SCRM: Shi's cervical rotational manipulation; BCM: basic cervical manipulation; VAS: visual analog scale; VSS-C: vertigo symptoms scale-Chinese version; HVLA: high velocity and low amplitude; SOP: standard operating procedure; RCT: randomized controlled trial; CT: computed tomography; ER: efficacy rate; NRS: numerical rating scale; CC: clinical improvement; CCs: clinical cureless; CR: clinical recurrence; AE: adverse events;

Author's contributions

ZD is the principal investigator and sponsor, who has initiated the current trial. ZD, RD and ZS conceived and designed the study. HS, YA, WY and HW executed the statistical methods and obtained ethical approval. ZD, ZS, HZ, and GL drafted the article or revised it critically for important intellectual content. ZD, RD and ZS reviewed and edited the manuscript. Final approval of the version to be published was agreed upon by all authors. The author(s) read and approved the final manuscript.

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Availability of data and materials

Not applicable

Ethics approval and consent to participate

Written informed consent will be obtained from all participants before enrolment in the study. The study design and procedure were approved by the IRB of Shanghai Baoshan Hosptial of Integrated Traditional Chinese and Western Medicine (Approval Number: 202218), and protocol version 1.0/20221201 is currently active.

Consent for publication

Authorship to the trial publications will be determined in accordance with the ICMJE recommendations.

Competing interests

The authors declare no competing interests.

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References

1. Zhang MC, Shi YY, Huang SR, Chen DY, Chen B, Wang X, Wang HH, Zhang KY, Guo K, Zhan HS. Study on the correlation between "Gucuofeng and Jinchucao" and cervical spondylosis. Zhongguo Gu Shang. 2013 Jul;26(7):557-60. Chinese. PMID: 24134023.
2. World Health Organization. ICD-11 For Mortality and Morbidity Statistics (Version: 09/2020). Geneva: World Health Organization; 2020 [cited 2020 Sep 18]. Available from https://icd.who.int/browse11/l-m/en.
3. Yuan WA, Zhang MC, Zhan HS. Understanding and diagnosis of "Gu Cuo Feng and Jin Chu Cao. Zhongguo Gu Shang. 2013 Jun;26(6):502-4. Chinese. PMID: 24015657.
4. Zhang KY, Zhuang Y, Zhan HS, Zhang MC, Shi YY. Clinical application of non-collinear spinous process in the diagnosis of cervical vertebra "Gu Cuo Feng and Jin Chu Cao". Zhongguo Gu Shang. 2013 Jan;26(1):47-9. Chinese. PMID: 23617142.
5. Goel A. Atlantoaxial Instability: Evolving Understanding. Acta Neurochir Suppl. 2019;125:59-62. https://doi.org/10.1007/978-3-319-62515-7_9.
6. Carlesso LC, Macdermid JC, Santaguida PL, Thabane L. Determining adverse events in patients with neck pain receiving orthopaedic manual physiotherapy: a pilot and feasibility study. Physiother Can. 2013 Summer;65(3):255-65. https://doi.org/10.3138/ptc.2012-28.
7. Neal KM, Mohamed AS. Atlantoaxial rotatory subluxation in children. J Am Acad Orthop Surg. 2015 Jun;23(6):382-92. https://doi.org/10.5435/JAAOS-D-14-00115.
8. Yang ZM. A discussion on the existence of atlantoaxial subluxation. Chin J Surg. 2006 October;44(20):1369-1375 (Chinese).
9. Végh I, Harmat K, Gerlinger I. Cervicalis vertigo – létező kórkép vagy fikció? [Cervical vertigo - reality or fiction?]. Orv Hetil. 2019 Jun;160(25):967-972. Hungarian. https://doi.org/10.1556/650.2019.31409.
10. Li Y, Peng B. Pathogenesis, Diagnosis, and Treatment of Cervical Vertigo. Pain Physician. 2015 Jul-Aug;18(4):E583-95. PMID: 26218949.
11. Hutting N, Kerry R, Coppieters MW, Scholten-Peeters GGM. Considerations to improve the safety of cervical spine manual therapy. Musculoskelet Sci Pract. 2018 Feb;33:41-45. https://doi.org/10.1016/j.msksp.2017.11.003.
12. Bautista-Aguirre F, Oliva-Pascual-Vaca Á, Heredia-Rizo AM, Boscá-Gandía JJ, Ricard F, Rodriguez-Blanco C. Effect of cervical vs. thoracic spinal manipulation on peripheral neural features and grip strength in subjects with chronic mechanical neck pain: a randomized controlled trial. Eur J Phys Rehabil Med 2017;53:333-41. https://doi.org/10.23736/S1973-9087.17.04431-8.
13. Moser N, Mior S, Noseworthy M, Côté P, Wells G, Behr M, Triano J. Effect of cervical manipulation on vertebral artery and cerebral haemodynamics in patients with chronic neck pain: a crossover randomised controlled trial. BMJ Open. 2019 May 28;9(5):e025219. https://doi.org/10.1136/bmjopen-2018-025219.
14. Chang L, Wang H, Guo Y, Cai Z, Zhan H. Experimental and numerical analysis of biomechanical effects in cervical spine positioning rotation manipulation. Int J Numer Method Biomed Eng. 2022 Dec;38(12):e3651. https://doi.org/10.1002/cnm.3651.
15. Rodríguez-Sanz J, Malo-Urriés M, Corral-de-Toro J, López-de-Celis C, Lucha-López MO, Tricás-Moreno JM, Lorente AI, Hidalgo-García C. Does the Addition of Manual Therapy Approach to a Cervical Exercise Program Improve Clinical Outcomes for Patients with Chronic Neck Pain in Short- and Mid-Term? A Randomized Controlled Trial. Int J Environ Res Public Health. 2020 Sep 10;17(18):6601. https://doi.org/10.3390/ijerph17186601.
16. Demoulin C, Baeri D, Toussaint G, Cagnie B, Beernaert A, Kaux JF, Vanderthommen M. Beliefs in the population about cracking sounds produced during spinal manipulation. Joint Bone Spine. 2018 Mar;85(2):239-242. https://doi.org/10.1016/j.jbspin.2017.04.006.
17. Ernst E. Chiropractic: a critical evaluation. J Pain Symptom Manage. 2008 May;35(5):544-62.

https://doi.org/10.1016/j.jpainsymman.2007.07.004.
18. Deng Z, Shen ZB, Zhan HS, Chen B, Lian YZ, Shang HB, Li GZ, Wang HH. Therapeutic effect of Shi's Rotation Manipulation Treatment for Cervical Spondylotic Radiculopathy. Zhong Guo Zhong Yi Gu Shang Ke Za Zhi. 2020 May 28(5):5-9. (Chinese)
19. Deng Z, Niu W, Wang H, Zhan HS. Biomechanics applied in traditional Chinese traumatology manipulation for treating cervical spine diseases. Journal of Medical Biomechanics, 2015 December 30(6):569-573. https://doi.org/10.3871/j.1004-7220.2015.06.569.
20. Deng Z, Wang K, Wang H, Lan T, Zhan H, Niu W. A finite element study of traditional Chinese cervical manipulation. Eur Spine J. 2017 Sep;26(9):2308-2317. https://doi.org/10.1007/s00586-017-5193-5.
21. Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586
22. Scudds RA. Pain outcome measures. J Hand Ther. 2001;14(2):86–90. https://doi.org/10.1016/S0894-1130(01)80038-7.
23. Deng Z, Yuan WA, Wang HH, Zhan HS. Development of Chinese version vertigo symptom scale (VSS): reliability and validity. Zhejiang Da Xue Xue Bao Yi Xue Ban. 2015 Mar;44(2):138-44. Chinese. https://doi.org/10.3785/j.issn.1008-9292.2015.03.004.
24. Bogduk N, Mercer S. Biomechanics of the cervical spine. I: Normal kinematics. Clin Biomech (Bristol, Avon). 2000 Nov;15(9):633-48. https://doi.org/10.1016/s0268-0033(00)00034-6.
25. Gross A, Langevin P, Burnie SJ, Bédard-Brochu MS, Empey B, Dugas E, Faber-Dobrescu M, Andres C, Graham N, Goldsmith CH, Brønfort G, Hoving JL, LeBlanc F. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. Cochrane Database Syst Rev. 2015 Sep 23;(9):CD004249. https://doi.org/10.1002/14651858.CD004249.
26. Huang F, Zhao S, Dai L, Feng Z, Wu Z, Chen J, Guo R, Tian Q, Fan Z, Wu S. Tuina for cervical vertigo: A systematic review and meta-analysis of randomized controlled trials. Complement Ther Clin Pract. 2020 May;39:101115. https://doi.org/10.1016/j.ctcp.2020.101115.
27. Reid SA, Rivett DA, Katekar MG, Callister R. Comparison of mulligan sustained natural apophyseal glides and maitland mobilizations for treatment of cervicogenic dizziness: a randomized controlled trial. Phys Ther. 2014 Apr;94(4):466-76. https://doi.org/10.2522/ptj.20120483.
28. Yao M, Tang ZY, Cui XJ, Sun YL, Ye XL, Wang P, Zhong WH, Zhang RC, Li HY, Hu ZJ, Wang WM, Qiao WP, Li J, Gao Y, Shi Q, Wang YJ. Shi-Style Cervical Mobilizations Versus Massage for Cervical Vertigo: A Multicenter, Randomized, Controlled Clinical Trial. J Altern Complement Med. 2020 Jan;26(1):58-66. https://doi.org/10.1089/acm.2019.0113.

Appendix 1

Table1 Flowchart schedule

Time-window	Visit 0 Screening stage (-3~0 day)	Visit 1 Week 4	Visit 2 Week 8	Visit 3 Week 12	Visit 4 Week 16	Visit 5 Week 20	Visit 6 Week 24
Registration and evaluation projects							
Baseline information	●						
Basic medical history and drug combination	●						
Inclusion and exclusion criteria	●						
Informed consent	●						
Randomization allocation	●						
Symptoms and signs	●	●	●	●	●	●	●
Cervical mobility examination and measurement	●	●	●	●	●	●	●
VAS scores	●	●	●	●	●	●	●
VSS-C scores	●	●			●		●
Imaging (CT or X ray)	●	●					●
Efficacy evaluation		●					●
Adverse events		●	●	●	●	●	●

Appendix 2

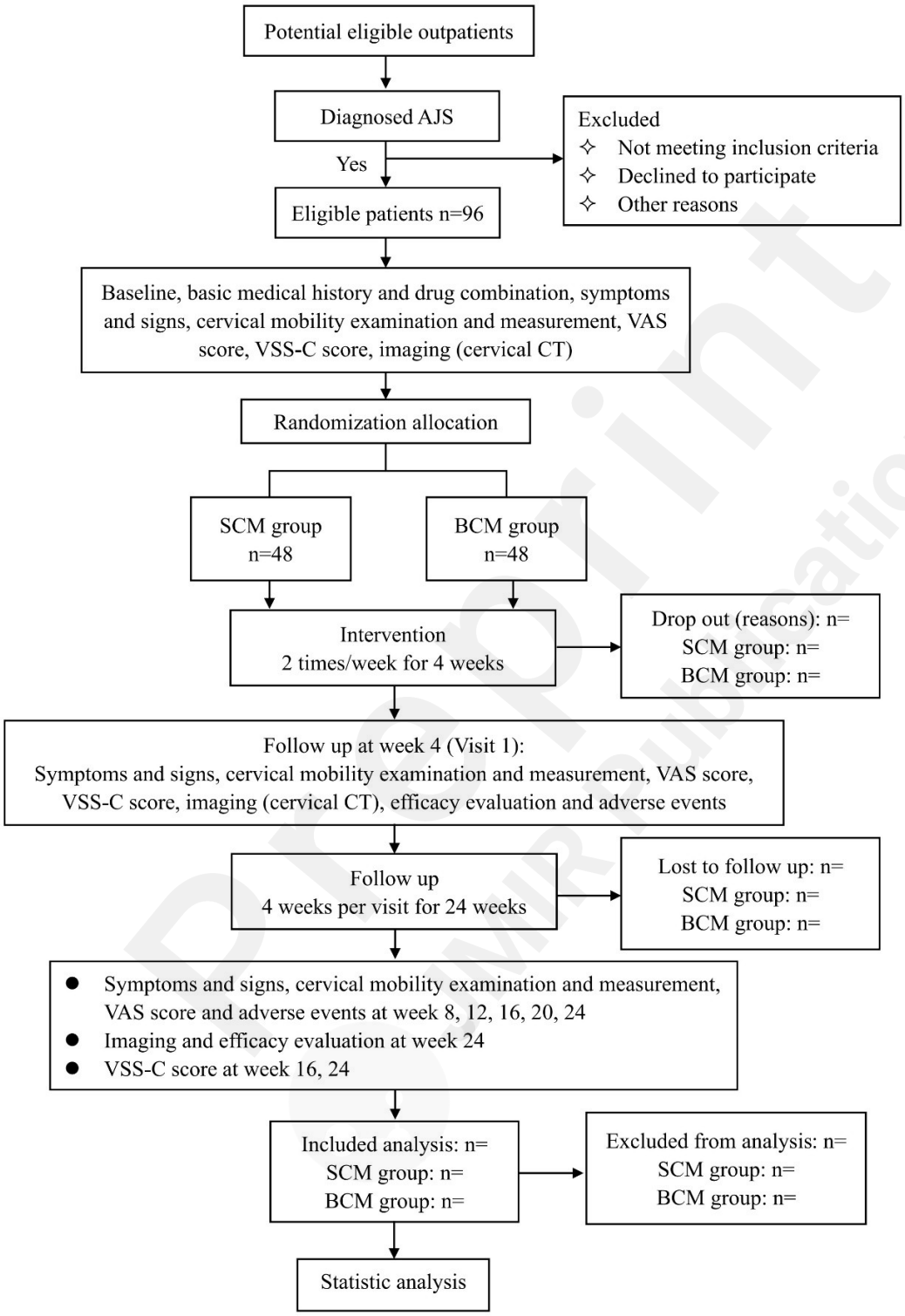


Fig. 1 Flow diagram of participants

Appendix 3

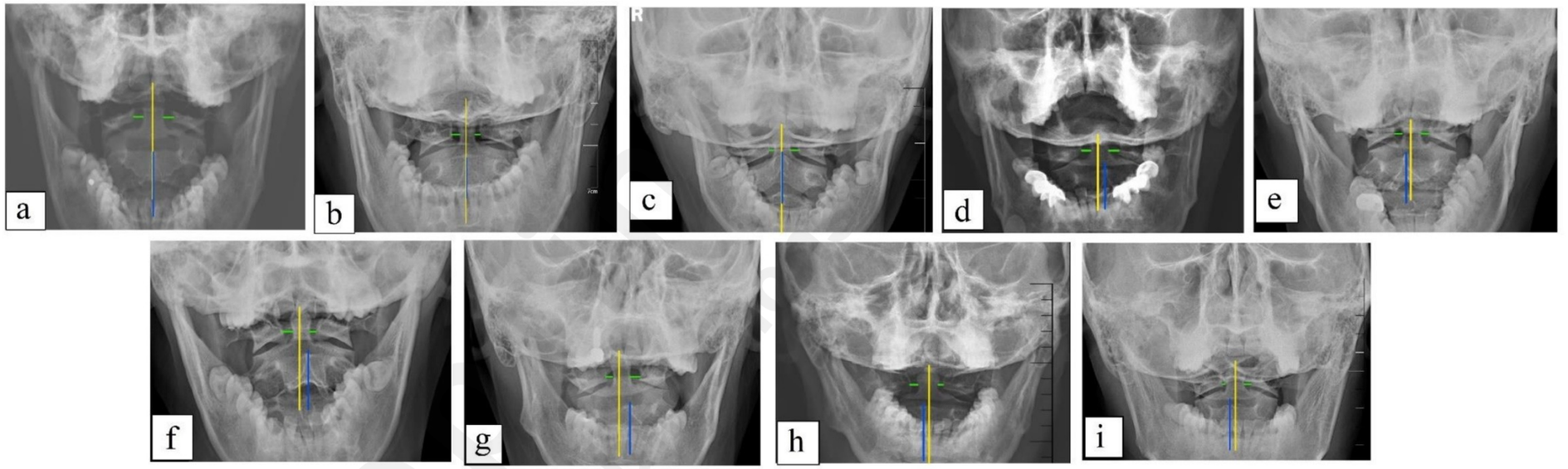
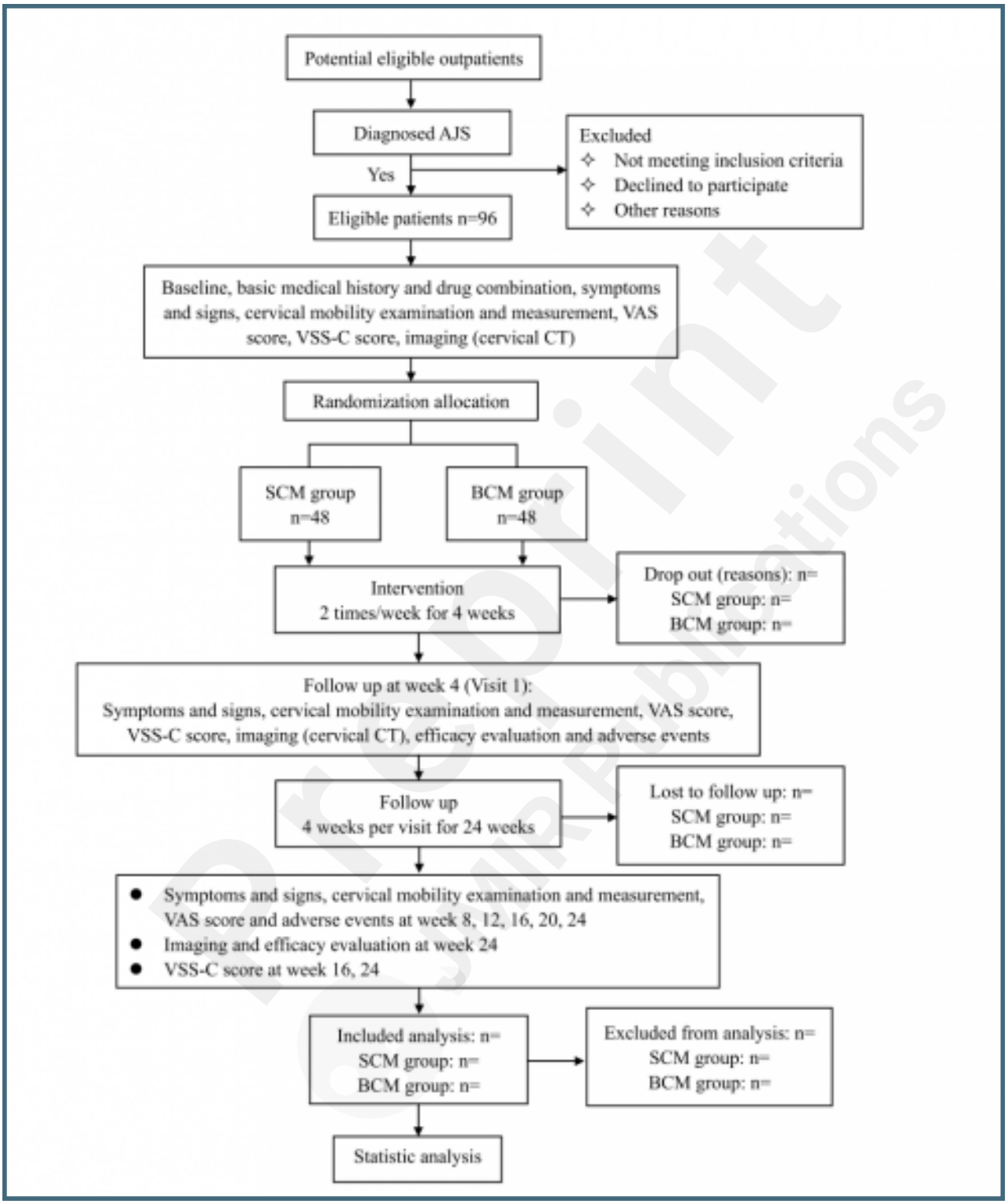


Fig.2 Comprehensive classification of AJS under X-ray (green lines: distance between the lateral mass of the atlantoaxial joint and the odontoid process; blue line: axis line of C2 spinous process; yellow line: the midline of the spinous process; a: The normal atlantoaxial joint; b:Type A; c: Type B; d: Type C; e: Type D; f: Type AC; g: Type AD; h: Type BC; i: Type BD)

Supplementary Files

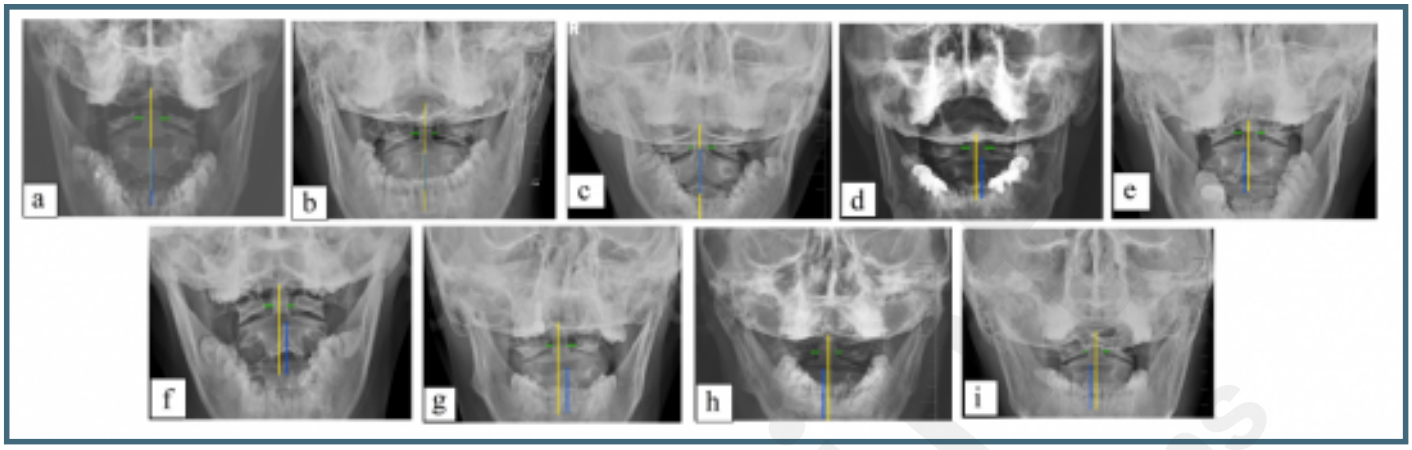
Figures

Flow diagram of participants.



Please Select A Types

Comprehensive classification of AJS under X-ray?green lines:distance between the lateral mass of the atlantoaxial joint and the odontoid process;blue line:axis line of C2 spinous process;yellow lines:the midline of the spinous process;a:The normal atlantoaxial joint;b:Type A;c:Type B;d:Type C;e:Type D;f:Type AC;g:Type AD;h:Type BC;i:Type BD?.



CONSORT (or other) checklists

SPIRIT checklist.
URL: http://asset.jmir.pub/assets/a1a78f6c5b94719164afb97522a0437c.pdf