

Title:

In-plane versus Real-time bi-plane Single-operator Laser-assisted with a innovative T-shaped probe for ultrasound-guided internal jugular vein catheterization: A Randomized Clinical Trial

Protocol Number: 2025-169

(Version: 3.0 Date: 2024-12-26)

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Researcher's Declaration and Protocol Signature Page

As the principal investigator of this research project, I will adhere to the Ministry of Health's 'Measures for the Ethical Review of Biomedical Research Involving Human Subjects' (2016), the WMA's Declaration of Helsinki (2013), the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002) and the ethical principles of Good Clinical Practice (GCP). Under the guidance of the Good Clinical Practice (GCP) guidelines, I will conduct the study in accordance with the protocol approved by the Ethics Committee and the requirements of this protocol, to ensure the scientific rigour of the study and to protect the health and rights of the research participants.

Principal Investigator: _____

Signature: _____

Date: _____

Synopsis

Title	In-plane versus Real-time bi-plane Single-operator Laser-assisted with a innovative T-shaped probe for ultrasound-guided internal jugular vein catheterization: A Randomized Clinical Trial
Version/Date	3.0 / 26 December 2024
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Study Objective	A Comparison of Success Rates and Safety of Internal Jugular Vein Catheterisation Under the Innovative T-shaped probe Ultrasound Guidance and Traditional Ultrasound Guidance
Sample Size	108
Study Subjects	Surgical patients aged 18 and over requiring central venous catheterisation

Inclusion Criteria	<ol style="list-style-type: none"> 1. Patients fully understood the benefits and risks of the study, voluntarily participated, and signed the informed consent form. 2. Require internal jugular vein catheterization. 3. ASA grade I~IV. 4. Over 18 years and older.
Exclusion Criteria	<ol style="list-style-type: none"> 1. Congenital malformation or abnormal development of the internal jugular vein. 2. Patients with peripheral vascular disease at the puncture site or cardiogenic shock. 3. Puncture site injury, infection, or hematoma.
Criteria for Ending	The postoperative day 1 follow-up is complete.
Primary Outcome	First-attempt Success Rate of RIJV Catheterization
Secondary Outcomes	<p>first-attempt puncture success rate, first-attempt catheterisation success rate, overall catheterisation success rate, first-attempt needle tip positioning score, first-attempt needle tip midpoint placement rate, number of needle direction adjustments, total number of puncture attempts, time for initial localization, total time for successful catheterisation, mechanical complications</p>

	incidence rate
Research Progress Program	Anticipated date of first subject enrollment: January 2025 Anticipated date of last subject enrollment: June 2025 Anticipated date of study completion: December 2025

List of Abbreviations

ASA	American Standards Association
CVC	Central Venous Catheterisation
SV	Subclavian Vein
FV	Femoral Vein
IJV	Internal Jugular Vein
IJVC	Internal Jugular Vein Catheterisation
RIJV	Right Internal Jugular Vein
MAP	Mean Arterial Pressure
ECG	Electrocardiogram
PETCO ₂	End-tidal Carbon Dioxide
BIS	Bispectral Index
V _t	Tidal Volume
PEEP	Positive End-expiratory Pressure
FiO ₂	Inspired Oxygen Concentration
I:E	Inspiratory-to-expiratory Ratio
MAC	Minimum Alveolar Concentration

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1. Background

Central venous catheterisation (CVC) is a common clinical procedure for deep vein puncture and is one of the essential skills for every anaesthetist and critical care physician. Common puncture sites include the internal jugular vein(IJV), subclavian vein(SV) and femoral vein(FV) ^[1]. However, the internal jugular vein is the site of choice due to its superficial location, relatively fixed anatomical position, minimal influence from respiratory movements, and low overall complication rate. CVC has a wide range of applications and is frequently used for rapid blood and fluid transfusion, the administration of highly irritating drugs, and intraoperative haemodynamic monitoring ^[2].

CVC placement is an invasive procedure involving complex techniques, its success requires not only precise vascular localisation but also the smooth insertion of the guidewire and catheter. Failure of CVC can result in a range of complications, such as arterial puncture, nerve injury, pneumothorax, chylothorax, arrhythmia, cardiac tamponade, and even death ^[3-6]. In pursuit of success, safety, and the minimisation of puncture injuries and complication rates, CVC insertion techniques are constantly being refined. Currently, the mainstream CVC insertion methods include traditional anatomical localisation, ultrasound localisation, and ultrasound-guided techniques ^[7]. The traditional anatomical landmark

method involves blind puncture based on palpation of arterial pulsations; it requires the operator to have extensive experience in blind puncture. Furthermore, when anatomical structures are abnormal, this method increases the difficulty of puncture, as well as the incidence of complications and failure rates. The ultrasound localisation method involves using ultrasound to scan the target vein prior to puncture, marking the superficial projection of the vein to guide the puncture site. This method allows for the identification of anatomical variations in advance and increases the accuracy of vein localisation. However, if the vein shifts during the procedure, the superficial landmarks will also change, making it impossible to guarantee the success rate of the puncture. In 1986 Yonei et al. first described ultrasound-guided central venous catheterisation, this technique has since been extensively studied and applied in various clinical settings [8]. The traditional ultrasound guidance method employs the short-axis out-of-plane technique, where in the long axis of the ultrasound probe is positioned perpendicular to the vertical of the internal jugular vein, projecting a transverse cross-section of the vein onto the centre of the ultrasound image. The vein appears as a circular structure on the image and can be compressed with slight pressure. The puncture needle is inserted at an angle of $30 - 45^{\circ}$ relative to the midpoint of the ultrasound probe's long axis at the point of skin contact. On the ultrasound image, the needle appears as a hyperechoic point.

Under ultrasound guidance, the target vessel is approached and punctured. Once backflash blood flow is observed, a guidewire is inserted, followed by the venous catheter. This method significantly improves the success rate of first-attempt CVC placement and reduces the incidence of associated complications. In 2002, the National Institute for Clinical Excellence (NICE) recommended that ultrasound-guided central venous catheterisation should be the method of choice for establishing central venous access in both adults and children ^[9].

Azmat et al. ^[10] randomised 200 patients into the ultrasound-guided group or the surface landmark group, the time taken to access a vein was significantly shorter in the real-time ultrasound-guided group than in the surface landmark group [(34.95 ± 11.47) s vs (146.59 ± 40.20) s], and the success rate of first-attempt catheterisation was also significantly higher (99% vs 89%). Furthermore, carotid artery puncture (9% vs 1%) and haematoma formation (7% vs 0%) were more common in the surface landmark group than in the ultrasound-guided group. The meta-analysis conducted by Wu et al. ^[11] included 26 randomised controlled trials (RCTs) involving 4,185 patients (2,081 receiving ultrasound guidance CVC and 2,104 receiving surface landmark CVC). The results showed that the catheterisation failure rate was reduced by 82% in the ultrasound-guided group, and the incidence of mechanical complications

such as arterial puncture, haematoma, pneumothorax and haemothorax was also significantly reduced. Furthermore, many similar studies [12–15] have also demonstrated that the use of ultrasound guidance leads to similar improvements in the success rate of central venous catheterisation and the incidence of complications, as well as corresponding improvements in the time taken for the needle to enter the vein and the number of puncture attempts.

The key difference between T-shaped ultrasound and traditional ultrasound methods lies in the probe. Traditional ultrasound probes are transverse-view probes. During puncture, the short-axis out-of-plane puncture method is commonly used, which can only display transverse ultrasound images of the vein and cannot visualise the guidewire or catheter as they enter the vessel. The T-shaped probe is an ultrasound method that combines short-axis and long-axis views. It allows for venous puncture guidance in the short-axis plane and the placement of guidewires and catheters in the long-axis plane, thereby maximising visualisation during the procedure and reducing the risk of complications associated with guidewire and catheter placement.

2. Trial Objective

To compare the first-attempt success rate and safety of central venous catheterisation under the innovative T-shaped probe ultrasound guidance

and traditional ultrasound guidance.

3. Selection of Subjects

3.1 Inclusion

3.1.1 Patients fully understood the benefits and risks of the study, voluntarily participated, and signed the informed consent form.

3.1.2 Require internal jugular vein catheterization.

3.1.3 ASA grade I~IV.

3.1.4 Over 18 years and older.

3.2 Exclusion

3.2.1 Congenital malformation or abnormal development of the internal jugular vein.

3.2.2 Patients with peripheral vascular disease at the puncture site or cardiogenic shock.

3.2.3 History of surgical intervention in the right neck region. Puncture site injury, infection, or hematoma.

4. Trial Design

4.1 Flow Diagram (Figure 1.)

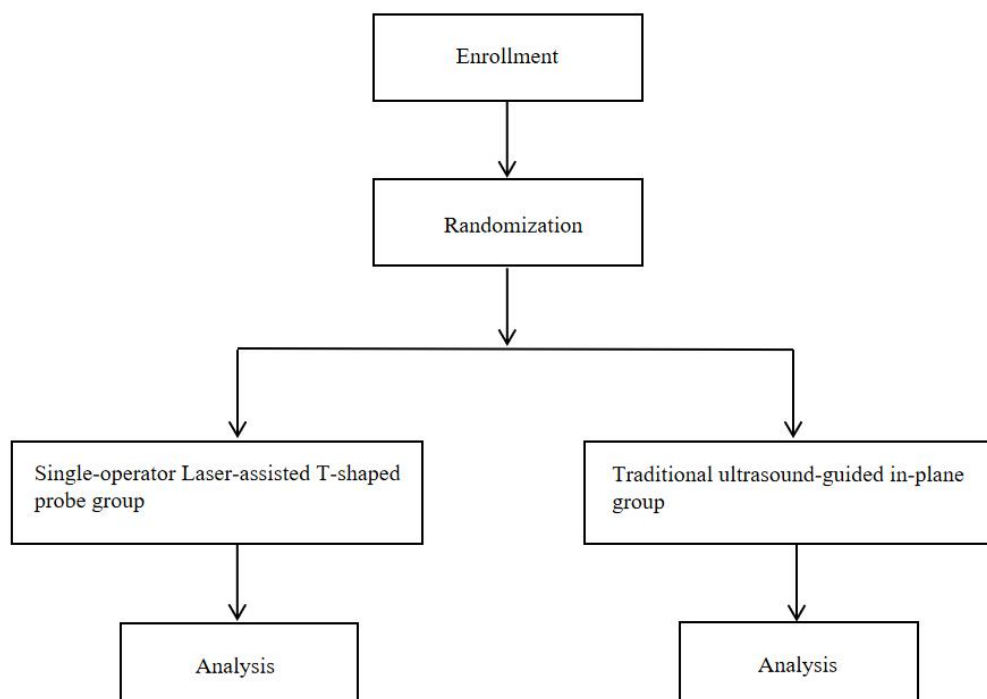


Figure 1.

4.2 Trial Hypotheses: We proposed that the use of Single-operator Laser-assisted T-shaped probe can improve the first-attempt success rate of guidewire insertion during internal jugular vein catheterisation(IJVC).

4.3 Sample Size Calculation

A review of the literature revealed that, in adult patients, the first-attempt success rate for ultrasound-guided central venous catheterisation was 77%. A pilot study involving 10 cases showed a first-attempt success rate of 98% for T-ultrasound-guided central venous catheterisation. Using PASS 21.0 (NCSS, USA) to calculate the sample size, with a significance level of $\alpha = 0.05$ and a power of $1 - \beta = 0.95$, and taking into account a

10% dropout rate, the required sample size was calculated to be 106 cases. Taking into account the implementation of a block randomisation method, the final sample size was set at 108 cases.

5. Randomization and Blind Method

5.1 Randomization

In this trial, patients will be randomly divided into two groups

Single-operator Laser-assisted T-shaped probe group and Traditional ultrasound-guided in-plane group in a 1:1 ratio.

Use a random number generator website (<https://www.randomizer.org>) to generate random numbers. Set the block size to 4. The allocation results were sealed in opaque, numbered envelopes.

5.2 Blind Method

5.2.1 Single-blind: In view of the notably different settings of the two techniques, the allocation was not blinded to the operators, equipment assistant, and research assistant. However, as all procedures were performed under anaesthesia, the study was conducted in a single-blind manner to the participants.

5.2.2 The operator team that was not involved in any other part of the study, consisted of doctor A and doctor B.

5.2.3 The equipment assistant is responsible for preparing the equipment

and assisting the operator during the procedure.

5.2.4 The research assistant is responsible for maintaining and distributing randomised numbers and coordinating communication between researchers. All data were collected and analyzed by the research assistant.

5.2.5 The statistician responsible for analysing the data were unaware of the allocation.

6. Trial Procedure

6.1 Screening

Surgical patients aged 18 and over requiring central venous catheterisation should be assessed for inclusion and sign informed consent. Screening should be completed prior to randomization.

6.2 Administration of Anesthesia

Patients were positioned supine, peripheral veins were cannulated, and routine monitoring of electrocardiogram (ECG), blood pressure, pulse oximetry, end-tidal carbon dioxide (PETCO₂) and Bispectral Index (BIS) was initiated.

All patients underwent the following anaesthetic induction protocol: intravenous administration of remimazolam 5 mg, sufentanil 0.3 µg/kg, propofol 2.5 mg/kg, and rocuronium 0.6 mg/kg. Once the muscle

relaxants had taken full effect, a standard-sized endotracheal tube was inserted via video laryngoscopy. Following successful intubation, the patient was connected to the anaesthesia machine. The tidal volume (V_t) was set to 6 ml/kg, positive end-expiratory pressure (PEEP) to 5 cmH₂O, inspired oxygen concentration (FiO_2) to 60%, and the inspiratory-to-expiratory ratio (I:E) to 1:2. The respiratory rate was adjusted to maintain PETCO₂ between 35 and 45 mmHg. Administer 1 MAC of sevoflurane by inhalation, and continuously infuse propofol at 0.6–1.2 mg/(kg·h) and remifentanyl at 0.02–0.15 µg/(kg·h) intravenously to maintain a BIS score of 40–60. During anaesthesia, vital signs were maintained at $\pm 20\%$ of baseline levels according to the anaesthetist's experience, with intermittent bolus doses of rocuronium 0.15 mg/kg administered as required during surgery.

After general anaesthesia and endotracheal intubation, all patients were placed in a Trendelenburg position with the head lowered by 15°, a thin pad is placed under the right shoulder to tilt the head 30° to the left and slightly extend the neck, fully exposing the puncture site. Select the appropriate ultrasound system and probe according to the group allocation (the Single-operator Laser-assisted T-shaped probe group and the traditional ultrasound-guided in-plane group). The ultrasound probe is gently placed against the skin without applying downward pressure to scan for the maximum transverse section of the right internal jugular vein,

and a mark is made at this point using a marker pen. Select a disposable central venous puncture kit for adults (18 G needle ,1.3 × 1.06 × 65 mm, 7 Fr 20 cm with 0.035 Inch guidewire Disposable Central Venous Catheter Set, ABLE, Guangdong Baihe Medical Technology Co. LTD). The operator should perform hand disinfection, put on sterile gloves, then disinfect the patient's skin and lay out a sterile drape.

6.3 Trial Equipments

6.3.1 Single-operator Laser-assisted with a innovative T-shaped probe

The Single-operator Laser-assisted T-shaped probe consisted of TUORen Ultrasonic System (TUR200, Shenzhen Tuoren Bio-Medical Electronics Co., LTD) with a T-shaped probe (L38T7C), a 3D-printed probe-carrying enclosure with a linear laser transmitter (ZLM120AL650-22130BXS, Shenzhen Zhonglai Technology Co., Ltd.) and ultrasonic probe manipulator.

6.3.2 Traditional Ultrasound System

Ultrasonic (Huasheng Color Ultrasonic Diagnostic System, Navis, Shenzhen Huasheng Medical Technology Co., LTD.) and a 4.0MHz phased probe were used for the long-axis in-plane internal jugular vein catheterization.

6.4 The Single-operator Laser-assisted T-shaped probe group:

The research assistant applies appropriate amount of coupling agent evenly to the ultrasound probe. The operator and assistant work together

to cover the 3D-printed manipulator arm and the entire ultrasound probe with a sterile sleeve, extrude air bubbles from between the probe and the sleeve, and apply coupling agent evenly to the outer surface of the sterile sleeve where it contacts the patient's skin to complete the preparation of the equipment.

To begin positioning, the operator uses the manipulator arm to gently place the T-shaped ultrasound probe against the patient's neck, positioning the short axis towards the head and the long axis towards the feet. The manipulator arm and rotation axis are adjusted so that the midline of the short-axis image passes through the centre of the internal jugular vein's transverse cross-section. At this point, the laser beam indicates the path to the centre of the internal jugular vein on the body surface, coinciding with the midline of the long-axis probe. After adjusting the rotation axis so that the midpoint of the short-axis probe aligns with the mark, slide the probe 1 cm further towards the head to ensure that the needle tip is closer to the maximum transverse cross-section when puncturing, positioning is then complete.

Once the arm is fixed to ensure the probe remains stable against the skin surface, this creates a hands-free, stable ultrasound guidance system that allows for continuous monitoring throughout the procedure. The operator should stabilise the skin near the puncture site with the left hand, holding

the puncture needle at a 45° angle to the skin with the right hand. The needle should be aligned with the laser path and inserted closely alongside the short-axis probe's 'mark' point. Once the needle tip has entered the subcutaneous tissue, we can see the needle tip on both in-plane and out-of-plane real-time ultrasound images, which helps us to determine whether the needle is placed above the highest point of the vein and whether the angle is appropriate. Once the short-axis and long-axis ultrasound images confirm that the needle has entered the vessel and unobstructed, non-pulsatile venous blood is pulled into the syringe, adjust the needle tip to the centre of the longitudinal section of the internal jugular vein based on the long-axis view. Subsequently, holding the needle in position with the left hand, slide the probe towards the feet with the right hand and, using the short-axis view, determine the needle tip position prior to guidewire insertion using the 'dynamic needle tip method'; capture a screenshot for scoring the needle tip position during this first-attempt. Maintain the needle tip position, insert the guidewire 30 cm without resistance through the syringe. Guided by the guidewire, advance the internal jugular vein catheter 12–15 cm. If resistance is still encountered, withdraw the guidewire, adjust or withdraw the needle from the internal jugular vein and apply pressure to the puncture site with sterile gauze. After approximately 3 minutes, when there is no significant bleeding at the puncture site, proceed to the next attempt. During this

process, the timer is not paused, the number of ultrasound probe repositionings and the number of needle direction adjustments are recorded throughout. If the third-attempt failed or took longer than 10 minutes, a senior physician selected an appropriate technique based on experience or changed the site to complete the central venous catheterization.

6.5 The traditional ultrasound-guided in-plane group:

The assistant applies coupling agent to the surface of the ultrasound probe. Working together, the operator and assistant cover the probe with a sterile sleeve, extrude air bubbles from between the probe and the sleeve, and apply coupling agent evenly to the outer surface of the sleeve to complete the preparation of the equipment.

To begin positioning, the operator holds the ultrasound probe in their left hand so that its long-axis midline is parallel to the vertical of the internal jugular vein. Once the midpoint of the probe's long-axis surface aligns with the 'mark' point, the probe is slid 1 cm further towards the head along the long-axis midline to ensure that the needle tip is as close to the maximum transverse cross-section when puncturing. The ultrasound probe is then held steady with the left hand, and positioning is complete.

Hold the puncture needle in the right hand at a 45° angle to the skin, insert the needle closely following the midpoint of the ultrasound probe's

long axis. Once the needle tip has entered the subcutaneous tissue, if the insertion trajectory appears deviated on the long-axis ultrasound image, adjust the insertion angle or reposition the probe to ensure the needle tip enters directly above the internal jugular vein. Once the ultrasound image confirms entry into the vessel and the syringe shows unobstructed venous blood, adjust the needle tip position so that it is situated at the mid-level of the long-axis section of the internal jugular vein. At this point, keep the right hand steady holding the puncture needle, whilst the left hand holds the ultrasound probe to determine the needle tip position prior to guidewire insertion using the 'dynamic needle tip method' via the short-axis view; save a screenshot for scoring the needle tip position during the first attempt. During this attempt, the needle tip is not repositioned; a guidewire is advanced 30 cm without resistance through the syringe. Under the guidance of the guidewire, an internal jugular vein catheter is inserted 12–15 cm and securely fixed. If significant resistance is encountered during guidewire insertion, the guidewire is withdrawn and reinserted after adjusting the intravascular positions of the needle tip. If resistance persists, withdraw the guidewire and the puncture needle from the internal jugular vein and apply pressure to the puncture site with sterile gauze. After approximately 3 minutes, when there is no significant bleeding at the puncture site, proceed to the next attempt. During this process, the operation timer is not paused, the number of ultrasound

probe repositionings and the number of needle direction adjustments are recorded throughout. If the third-attempt failed or took longer than 10 minutes, a senior physician selected an appropriate technique based on experience or changed the site to complete the central venous catheterization.

6.6 Data Record

6.6.1 Basic Characteristics

From the patient's entry into the operating room, the research assistant is responsible for recording the following data in the CRF: age, sex, height, weight, type of surgery, ASA grade, pre-procedure mean arterial pressure (MAP), coagulation function, sternoclavicular distance, neck circumference, anteroposterior diameter, depth of the internal jugular vein and common carotid artery coverage rate.

6.6.2 Outcomes

From the preparation for catheterization until the completion of follow-up, the research assistant is responsible for recording the following data in the CRF: success of the first-attempt catheterization, success of the first-attempt puncture, first-attempt needle tip positioning score, number of ultrasound probe repositionings , number of needle direction adjustments, total number of puncture attempts, time for equipment

preparation, time for initial localization, time for successful guidewire insertion, total time for successful catheterization and occurrence of complications (posterior wall puncture of the internal jugular vein, arterial puncture, haematoma, haemothorax, pneumothorax, nerve injury, internal jugular vein thrombosis) .

6.7 Operators Training and Standardization

The operators are selected from the Department of Anaesthesia at the First Hospital of Jilin University and comprise two residents (clinical anaesthesia year 3) and two attending anaesthesiologists (clinical anaesthesia year 5–10). All selected clinicians have a minimum of 50 independently performed cases of ultrasound-guided central venous catheterisation in adults.

Prior to the commencement of the study, all operators completed a specially designed training programme under the supervision of the principal investigator (Senior Consultant). This programme comprised basic theory, literature reviews, video-based learning, followed by a theoretical assessment, manikin-based practice and assessment, and a practical assessment, ensuring that all operators achieved a proficient level of mastery in both techniques.

7. Endpoints

7.1 Primary Endpoint

First-attempt Success of RIJV Catheterization: In cases where the initial puncture and catheterisation attempts were both successful, the case is considered a successful first-attempt catheterisation .

7.2 Secondary Endpoints

First-attempt Puncture Success: During the first attempt puncture, the ultrasound scan shows that the needle tip is in the vein, and unpulsatile blood flow is visible in the syringe, the case is considered a first-attempt success puncture.

First-attempt Catheterisation Success: The initial attempt to insert the guidewire meet with no resistance, backflush of venous blood is observed through the venous catheter, and ultrasound confirms that the catheter is located in the vein.

Overall Catheterisation Success: Internal jugular vein catheterisation is considered success if the number of puncture attempts is no more than 3 and the time taken for puncture and catheter placement is less than 10 minutes.

First-attempt Needle Tip Positioning score: The position of the needle tip on the ultrasound image immediately upon the first attempt to insert the needle into the internal jugular vein under ultrasound guidance. (Figure 2.)

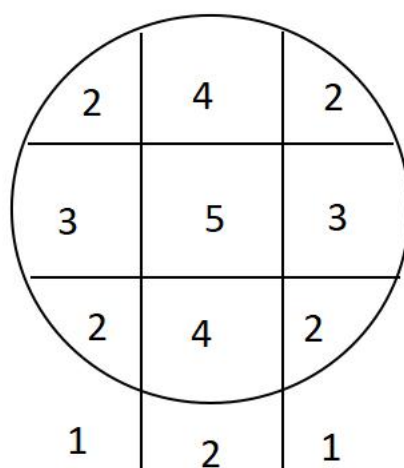


Figure 2. Divides the cross-section of the internal jugular vein into 12 quadrants, with each quadrant assigned a score based on its position, ranging from a minimum of 1 to a maximum of 5.

First-attempt Needle Tip Midpoint Placement Rate: The proportion of cases in this group where the first-attempt needle tip positioning score is 5.

Number of Needle Direction Adjustments: The number of adjustments made to the needle tip's direction from the moment the needle first penetrates the skin until the catheter is successfully placed.

Total Number of Puncture Attempts: A puncture attempt is defined as the period from the moment the operator inserts the needle into the skin until the needle is removed. The number of puncture attempts is the total number of attempts made from the start of the procedure until successful puncture.

Time for Initial Localization: The time taken from the moment the ultrasound probe first makes contact with the patient's neck until the optimal ultrasound image is obtained.

Total Time for Successful Catheterisation: The time taken from the first attempt to insert the needle into the skin until the successful placement of the intravenous catheter.

Mechanical Complications: Ultrasound examination during the internal jugular vein catheterisation procedure, immediately following successful placement, and during follow-up is used to detect complications associated with internal jugular vein catheterisation, including: puncture of the posterior wall of the internal jugular vein, arterial puncture, haematoma, haemothorax, pneumothorax, nerve injury, and internal jugular vein thrombosis.

8. Adverse events

8.1 Definition : An adverse event is any unexpected, unfavourable medical occurrence associated with any medical intervention in a study, regardless of whether it is related to the conduct of the trial. An adverse event may be any unexpected and undesirable symptom, sign or transient condition associated with the use of the product.

8.2 Monitoring, recording and management of adverse events: Adverse

events shall be monitored from the start of the puncture until its completion. Should an adverse event occur, the procedure shall be stopped immediately, symptomatic treatment administered without delay, and the event accurately recorded on the CRF form; monitoring shall continue until the event has completely resolved or treatment has been discontinued.

8.3 Definition of serious adverse events: A serious adverse event is defined as any unexpected medical event that results in death, is life-threatening, leads to prolonged hospitalisation, causes persistent or severe disability or functional impairment, or constitutes any other serious event. The monitoring period for serious adverse events extends from the start of the study intervention until the third day post-operation.

8.4 Reporting and Management of Serious Adverse Events

8.4.1 In the event of a serious adverse event, the procedure shall be stopped immediately and appropriate symptomatic treatment administered without delay.

8.4.2 In the event of a treatment-related death, the clinical trial shall be suspended immediately, reported to the Ethics Committee as soon as possible (within 24 hours), and the relevant data shall be recorded in detail and properly retained.

8.4.3 All serious adverse events shall be followed up until they are

satisfactorily resolved or the patient's condition has stabilised.

9. Unblinding

Once all enrolled cases have been processed, the case report forms have been entered and verified for accuracy, the data will be unblinded and submitted to the statistical analysts for analysis. The data will be re-unblinded once the statistical analysis has been completed.

10. Statistical Analysis Methods

Shapiro-wilk test was used to test the normality of measurement data. The measurement data with normal distribution were described by mean \pm standard deviation, and the measurement data with non-normal distribution were described by median (lower quartile, upper quartile). Count data were described by frequency (percentage). Independent t-test, χ^2 test were used to assess the baseline characteristics of the study population, and GLM analysis was used to adjust the effect of covariates; The main outcome measures were analyzed using the χ^2 test. Secondary outcomes were analyzed using the chi-square test, Fisher's exact test and Mann-Whitney U test. All statistical analyses were performed using IBM SPSS Statistics 24 (SPSS Corporation, IBM Corporation, USA). Statistical significance was defined as a two-sided P-value of less than 0.05.

11. Quality Control and Quality Assurance

11.1 Measures for Researchers and Clinicians

11.1.1 The clinical trial protocol should be explained in detail to researchers and clinicians prior to the commencement of the study, and must be strictly adhered to throughout the trial.

11.1.2 Researchers should complete the case report form fully, in detail and accurately. All observed results and adverse events during the clinical trial should be verified and recorded promptly and thoroughly to ensure the reliability of the data.

11.1.3 When summarising and analysing the results of clinical trials, standard statistical analysis methods must be employed, and this work must be carried out by professionals specialising in statistics.

11.1.4 All conclusions drawn from clinical trials must be derived from the original data.

11.2 Measures to Ensure Participants' Compliance

11.2.1 Each patient enrolled in the trial must be made fully aware of the potential benefits and risks associated with the investigational device.

11.2.2 Each enrolled patient must sign an informed consent form in person or through a representative.

11.2.3 During the trial, if a participant is found to refuse to use the investigational device, they shall be excluded from further participation in

the trial.

11.3 Termination of the Trial

11.3.1 If a procedure-related death occur during the trial, the trial should be terminated prematurely and reported promptly to the Ethics Committee. Resumption of the trial requires the approval of the Ethics Committee.

11.3.2 Under normal circumstances, once the enrolment and follow-up of all patients have been completed, the clinical trial may be terminated with the consent of the principal investigator.

12. Ethical Requirements

12.1 Clinical trials shall be conducted in accordance with the Declaration of Helsinki and relevant Chinese regulations on the management of clinical trials. Clinical trials may only be conducted after the trial protocol has been approved by the clinical research ethics committee prior to the commencement of the trial;

12.2 Prior to the enrolment of each subject in this trial, the investigator is responsible for providing a complete and comprehensive written explanation of the trial's objectives, content, and potential risks and benefits. Patients must be informed that they have the right to withdraw from the study at any time.

The investigator is responsible for obtaining informed consent from each patient prior to their enrollment into the trial. Each subject shall receive a copy of the informed consent form, which shall be retained as part of the clinical trial documentation for future reference. For the purposes of this trial, both the patient and their authorised representative (in the event the patient is under anaesthesia) shall be informed of the above details prior to surgery and shall sign the informed consent form and the power of attorney (using the hospital's standard form) as evidence.

12.3 The trial results will be published in the form of a research paper. However, all personal information relating to participants will be anonymised and treated as confidential.

13. Documents Retention

In accordance with GCP requirements, CRF forms must be retained for five years.

14. Institutional Review Board or EC/IEC

The protocol, any protocol amendments and consent form for the proposed clinical trial and any other documents required by the local IRB/EC/IEC must be submitted by the Investigator for review and approval to the IRB/EC/IEC. The Investigator must also ensure that the IRB/EC/IEC reviews the progress of the trial on a regular basis and

renews its approval of the study on an annual basis.

15. Reference

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