Midline Catheter Tip Positioning and Catheter-Related Complications during Antimicrobial Therapy: A Multicenter Randomized Controlled Trial

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Method

2.1 Study Design

This was a researcher-initiated, multicenter, randomized controlled trial conducted in six first-class general hospitals in China's Zhejiang, Fujian, Jiangsu, and Liaoning provinces. Twelve IV nurse specialists were involved in performing the catheterizations. The research protocol was based on assigning patients to three different catheter tip placement groups and observing the relationship between tip placement and catheter-related complications. The institutional review board approved the research protocol of each participating hospital according to the Helsinki Declaration that respects individuals and recognizes vulnerable groups. All the participants had the right to make informed decisions. (IRB:20200107-11). Patients who underwent MC placement in all six hospitals were enrolled, and the study was conducted between September 2020 and January 2021.

2.2 Participants

A fixed-point continuous convenience sampling method was adopted to enroll 330 participants. The participants who met the clinical criteria for this study were informed about the study and written informed consent was obtained from each participant. Consent may also have been obtained from legally authorized persons. The inclusion criteria were as follows ① estimated time of intravenous infusion ≥ 1 week before catheterization; ② age: ≥18 years; ③ antimicrobial therapy was only used for treatment during hospitalization, with a pH value of 5–9 and osmotic pressure< 900 mOsm/L; and ④ patients were conscious and able to communicate normally. ⑤ The catheter-to-vessel ratio is less than 45%. The exclusion criteria were as follows: ① a history of radiotherapy, thrombosis, and trauma at the catheterization site and ② plans to discharge with a catheter during the study duration. Withdrawal criteria were as follows: ① active discharge from the hospital during indwelling of the catheter; ② failure to be followed-up after catheterization due to disease; and ③ a change in health status during antimicrobial therapy treatment, requiring other drugs to be infused treatment through the MC.

2.3 Sampling

A general formula-based sample estimation method using the data on the relationship between MC tip position and catheter-related complications was used to calculate the sample size (Wu et al., 2020). Based on the selected reference, the incidence of complications at the tip of the MC at the thoracic wall of the axillary vein was 32.5% (Wu et al., 2020), while the incidence of complications in the subclavian vein was 12.5% (Wu et al., 2020). A power analysis was performed to calculate the effect size. Efficacy was set at 0.8 (with an 80% probability of finding a difference between populations) and 0.05 (5% of Type I error). Considering external factors that may have caused loss and withdrawal, each group was increased in size by 20%, to 65 patients per group.

2.4 Randomization and Grouping

There were 428 eligible patients, and 330 consented to participating in this study. A random sequence was generated after participants were recruited, and participants were randomized into three groups using a computerized random number generation

technique. Then, a proportional allocation of treatment methods was adopted to equalize the participants in all groups. Microsoft Excel generated 1000 random integers and 330 corresponding numbers were drawn. The 330 corresponding numbers were arranged into opaque and sequentially numbered envelopes. Then, the envelopes were sorted by random sequence and evenly distributed among the six selected hospitals. Three different study groups with equal numbers of participants (n=110) were established using this non-stratified random allocations.

2.4.1 Study Groups

1. Experimental Group 1 contained patients assigned with the numbers obtained after dividing the computer-generated random numbers by three, with a remainder of one.
2. Experimental Group 2 contained patients assigned with numbers obtained after dividing computer-generated random numbers by three, with a remainder of two.
3. The control group included patients assigned numbers obtained when the random numbers were divisible by three.

2.5 Intervention

Detailed history-taking, including medical history, and clinical exams were provided to all participants were, and written informed consent was obtained. A single-blind design was adopted, in which the participants did not know their inclusion status, or whether they were in the control or experimental groups. Double blinding was avoided due to ethical concerns and the questionable efficacy of the experiment. After obtaining informed consent from the patients, the project coordinators of each hospital opened the envelopes according to their serial number. They informed the catheterization nurse about the patient's inclusion status.

2.5.1 Catheter Pre-Placement Length Measurement and Evaluation of Tip Position

The measurement of catheter pre-placement length and the determination method of catheter tip position were formulated based on the *Consensus* (Bai & Guo, 2019), expert opinions on vascular anatomy, and relevant literature (Huang et al., 2018; Pathak et al., 2015; Sun et al., 2014). An intravenous therapy (IV) specialist nurse confirmed catheter tip positioning by ultrasound during catheterization, and the position of the catheter tip was adjusted according to ultrasound imaging. X-ray imaging was performed after catheterization to confirm the position of the catheter tip. The measurement methods for the tip position and pre-placement insertion length of the different groups of catheters were as follows:

(1) Experimental Group 1: The catheter tip was placed in the subclavian vein. The pre-placement catheter length measured through the body surface was greater than the actual length. Therefore, 2 cm was subtracted from the pre-puncture point to the ipsilateral sternoclavicular joint to calculate the effective catheter pre-placement length.

(2) Experiment Group 2: The tip of the catheter was placed in the axillary vein of the chest wall. The pre-placement length of the catheter was measured by subtracting 3–4 cm from the distance between the puncture point and ipsilateral midclavicular line.

This adjustment was intended to prevent the catheter tip from entering the subclavian vein.

(3) The control group: the catheter tip was located distal to the axillary vein. The measurement method of catheter pre-placement length was as follows: in cases where the catheter was punctured from the basilic and brachial veins, the distance from the pre-puncture point to the intermuscular sulcus of the ipsilateral deltoid muscle and pectoralis major muscle was measured (not surpassing the intermuscular sulcus and not reaching the axilla); however, the distance from the pre-puncture point to the ipsilateral sub shoulder or axilla was measured.

2.5.2 Catheter Insertion Procedure

A fixed routine for pre-insertion cleaning and equipment was followed, including hand washing, placing the patient in the supine position, skin antisepsis, and preparation of the sterile field. Catheter insertion was performed by senior nurses in the intravenous treatment room, which was a standardized setting for venipuncture. Conventional catheter placement and maintenance methods were adopted as follows: ① evaluation: physicians confirmed the condition of the pre-puncture intima through ultrasound before catheterization. If ultrasound imaging did not show endothelium abnormalities, such as rough intima, it was noted as a smooth standard. Subsequently, 12 catheterization nurses selected the puncture site guided by ultrasound. Nurses took 1/3 of the middle part of the patient's upper arm as the best puncture area and used ultrasound to measure the diameter of the vessel (Chen et al., 2018). ② Catheterization: each hospital assigned two senior IV nurses for MC puncture and measured the catheter pre-placement length according to the measurement method of different groups, and the catheter was placed using ultrasound-guided and modified Seldinger techniques. After confirming the position of the tip, the catheter was trimmed, and the extension sets was connected, with the length of the external catheter were3 cm. ③ Maintenance: 24 IV specialist nurses were trained to monitor and evaluate catheter functioning weekly, and clinical nurses conducted routine maintenance until study completion. Daily data were recorded and updated to computerized data records.

2.5.3 *Catheter Maintenance*

As suggested by the relevant literature, members of the research group designed the first draft of the MC tip positioning complication observation table. The observation table was later improved after modification by the IV specialist nurse of each hospital, and a third-party Statistics agent designed the electronic database for research. The collected data included the following two categories: ① baseline data of participants: age, sex, educational background, height, weight, diagnosis, history of thrombosis, surgical trauma, and chronic diseases, hemoglobin concentration, platelet count, white blood cell count, prothrombin time, activated partial thrombin time, history of CVC, PICC, and MC; ② Data on catheterization conditions: number of catheterizations, placement site, placement vein, and successful catheterization with the first attempt; ③ Data on the use and maintenance of catheters: daily catheter function evaluation, assessment of complications, and the time and reason of removal IV lines, and the types of antibiotics used in antimicrobial therapy.

2.6 Evaluation Indicators and Judgment Criteria

2.6.1 Incidence of Catheter-Related Complications

First, the catheter-related complications were assessed. The complications studied included phlebitis, catheter-related thrombosis, catheter occlusion, catheter dislodgement, bleeding, catheter-related infections, and infiltration. In this assessment, the incidence of each complication (i.e., number of patients with these complications) was divided by the total number of cases. Then, the total number of incidences of catheter-related complications was taken as the main outcome index (i.e., the number of patients with complications/the total number of patients). One patient with one or multiple complications was counted as one case in total.

The judgment criteria for each complication were as follows: ① phlebitis: the relevant contents in the Standard (Gorski et al., 2021) were considered; ② catheter-related thrombosis, also referred to as symptomatic thrombosis, was observed and reported either by patients or bedside nurses. Edema the limbs, neck, shoulder, chest, and/or face on the side of catheterization was observed for and reported to physicians, in order to perform an ultrasound for venous thrombosis detection; ③ catheter-related infections included local infection at the puncture site and catheter-related bloodstream infection, which were evaluated according to the corresponding diagnostic criteria in the Standard (Gorski et al., 2021); ④ catheter occlusion, inability to withdraw blood or sluggish blood return, sluggish flow; resistance or inability to flush lumen, inability to infuse fluid, Frequent occlusion alarms on electronic infusion pump. ⑤ catheter dislodgement included dislodgement of more than 3 cm; ⑥infiltration was noted when the puncture site had liquid exudation; and ⑦ bleeding referred to the blood exudation at the puncture site 48 h after catheterization.

2.6.2 Indwelling Catheter Duration

Indwelling catheter duration referred to the number of days between the date of catheter placement and removal.

2.7 Data Collection

Catheterization nurses recorded baseline data prior to catheterization, and only the most recent results were recorded one week prior to catheterization, when multiple laboratory results were available. Catheterization site evaluations were recorded after placement, and patients were followed up for 48 h after catheterization as well as every 7th day by IV specialist nurses to review and record the progress of antimicrobial therapy. The last follow-up was conducted at the time of removal, where the reason for removal was also recorded. In addition, bedside nurses evaluated and recorded catheter functioning and complications daily.

2.8 Quality Control

Quality standards and controls were maintained throughout the study. All hospitals included in this study used the same brand and batch number of silicone-valved catheters, with a total length of 30 cm. Catheters could be trimmed to ensure a consistent length of the external catheter and a unified catheter placement and maintenance process. The same criteria were used to appoint IV specialized nurses in each hospital. Only those who had more than three years of PICC or MC

placement experience and more than 200 cases of catheterization were assigned. After catheterization, the evaluation video for catheter-related complications was sent to the nurse managers of the department in which the participants were located. Bedside nurses were trained and assessed by a nurse manager in the department. Researchers with unified training collected the relevant data, followed up, and stored the data in a dedicated electronic database. One researcher was assigned to check the data entries from each hospital, and a third-party statistics agent rechecked all entries. In case of extreme or missing values, the data were rechecked by the project coordinator of each hospital.