Original Article

Modified Insertion Techniques Decreases the Risk of Tip Malposition in Peripherally Inserted Central Catheters: A Systematic Review and Meta-Analysis

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Abstract

Objectives: Traditional insertion technique of peripherally inserted central catheter (PICC) is associated with an increased risk of tip malposition. Several studies indicate that modified insertion technique may address this issue. However, a definitive conclusion was not obtained. A systematic review and meta-analysis was therefore performed to evaluate the effects of modified insertion technique versus traditional insertion technique in PICC.
Methods: PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), China Biomedical Database (CBM), Wanfang and China National Knowledge Infrastructure (CNKI) were searched to identify potential randomized controlled trials that compared modified with traditional insertion technique for PICC from inception through April, 2016. All statistical analyses were conducted by using Reviewer Manager (RevMan) 5.3. We also applied the GRADE method to grade the level of evidence.
Results: We included eventually 8 RCTs, comprising 1482 participants. The meta-analysis suggested that modified insertion techniques decreased the rate of malposition (8 RCTs, n = 1482, risk ratio [RR] 0.16, 95% confidence intervals [CIs] 0.10 to 0.26, moderate quality of evidence), shortened insertion time (2 RCTs, n = 388, mean difference [MD] -3.45, 95% CI -3.86 to -3.03, low quality of evidence), and improved the comfort level of participants (2 RCTs, n = 388, MD -1.61, 95% CI - 1.82 to -1.39, low quality of evidence).
Conclusions: Modified insertion technique is benefit for decreasing the rate of malposition, shortening insertion time, and improving the comfort level in PICC.

Keywords: Peripherally inserted central catheter; modified insertion techniques; malposition; systematic review; meta-analysis

Introduction

Peripherally inserted central catheter (PICC) is usually used to measure circulatory or heart functions, provide long-term access route for infusions and blood tests, and deliver drugs that require rapid dilution and contrast medium for cardiac imaging (Dale et al., 2016, Chopra et al., 2013). Furthermore, it is intended for patients requiring up to 12 months of intravenous injection (IV) therapy, which is the lack of needle sticks and placement at the bedside (Caparas et al., 2014, Schweickert et al., 2009). As a sort of central venous access PICC inserted from the veins of arm then threaded into the larger veins above the heart. Compared with other central catheters, PICC has been increasingly applied in clinical practice due to easing of insertion, perceived safety, and cost-effectiveness. Additionally, the proliferation of nurse-led PICC teams has made their use more convenient and accessible in many settings (Chopra et al., 2013). Although PICC technique has several advantages, it is associated with increased rates of complications, such as air embolism, infections, phlebitis, catheter malposition, thrombus formation, and difficult removal (Dennis et al., 1990). Of those complications, malposition was reported to have typically high rate during catheterization. Previous observational studies suggested that catheter tip malposition occur commonly in PICC, and the corresponding incidence varies from 10% to more than 60% (Obaid and Amerasekera, 2011, Schweickert et al., 2009). In terms of malposition, the incidence of ectopia in jugular vein can reach up to 36%, and even up to 64.1% in China (Jiang et al., 2011, Trerotola et al., 2007). Malposition during PICC may lead to catheter malfunction, cardiac arrhythmia or tamponade (Amerasekera et al., 2009). If the catheter remains in the jugular vein, patients would suffered from discomfort, difficulty in turning the head and neck, and soreness in the affected side (Moraza-Dulanto et al., 2012). The consequences of such malposition are at least a second procedure such as catheter withdrawal or repeat chest radiograph (if the infused solution is amenable to a midline catheter) (Schweickert et al., 2009), which can interrupt treatment, increase healthcare costs, morbidity as well as the risk of infection (Ma et al., 2010).

Along with the advances in PICC techniques (polyurethane compounds), radiographic devices (e.g. bedside ultrasound) were developed over recent these years, a number of insertion techniques appeared to reduce the incidence of catheter tip malposition. Head rotation to the side of cannulation has been a traditional sending method which needs patients turning head toward the insertion side and tilting the chin to the chest during catheter introducing after sheath tube stripping. Currently two modified sending methods have been used in clinical scenario: 1) withdrawing guide wire ahead while sending and 2) continuous slow saline injection during catheter advancement. Withdrawing guide wire ahead method modified sending technique while admitting the catheter in subclavian vein, retrieving guide wire 3~5cm, gently moved through the vein until the tip is in the adequate tip position. Continuous slow saline injection method needs assistant pulse injecting around 20ml saline with speed of 0.5~1cm/s during catheter advancement. Although the 3 methods have been applied in clinic, there is scarce evidence discussing which one to select. Therefore, we conduct a systematic review and meta-analysis to evaluate the efficacy of two modified sending methods compared to traditional sending method during PICC placement.

Methods

We designed and reported this meta-analysis in accordance with the recommendations of Cochrane handbook for systematic reviews of interventions (Higgins and Green, 2010) and preferred reporting item for systematic review and meta-analysis statement (PRISMA) (Moher et al., 2010). There was no formal protocol for this meta-analysis.

Search strategy

PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), China Biomedical Literature Database (CBM), Wanfang, and China National Knowledge Infrastructure (CNKI) were searched to identify the potential randomized controlled trials (RCTs) that compared modified with traditional insertion technique for PICC from inception through April 2016. We constructed sensitive search algorithms using exploded medical subject heading and full-text words, including “PICC”, “Peripherally Inserted Central Catheter”, “CVC”, “Central Venous Catheter”, “Central Vena Catheterization”, “ectopia”, “misplacement”, “dystopy”, “heterotopia”, “malposition”, “precaution”, “prevent*”, “avoid*”, “randomized controlled trial”, “randomized controlled trials as topic”, “random*”. The restrictions of language and publication status were not imposed. We also checked manually the reference lists of relevant reviews and included studies to capture additional potentially eligible studies.

Study selection

Two investigators (QL and MW) removed independently duplicate records, reviewed the eligibility through screening titles and abstracts, and identified remaining records to be as included, excluded or requiring further assessment. The published RCTs meeting the following criteria were included: (i) patients: adult patients scheduled to receive PICC in arm; (ii) intervention: modified insertion technique of PICC; (iii) comparison: traditional insertion technique of PICC; and (iv) one or more the following outcomes: malposition rate, insertion time, and conform level. We excluded studies that investigated the reasons of malposition (e.g. PICCs inserted into the leg), case reports of unusual techniques. Any discrepancies on eligibility of studies were resolved by consulting a third investigator (FJM).

Data extraction

Two independent investigators (QL and SZ) used a standardized Excel (Microsoft Corporation) file to extract the following information from each included study: first author, publication year, number of participants, methods used to generate random sequence, average age of participants, kind of diseases, details of intervention and control regimes and outcomes of interest. When we found duplicate reports of the same study in preliminary abstracts and articles, we analyzed data from the most complete dataset. Discrepancies were resolved by discussion between the two investigators.

Assessment of risk of bias

Two independent investigators (LY and XLZ) used the Cochrane risk of bias tool to assess the risk of bias of each included studies (Higgins et al., 2011). The following items were assigned a value of 'low', 'unclear', or 'high': random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting; and other bias. As dictated by the Cochrane method, trials were rated to be low risk of bias when all key domains are valued low, while trials were rated to be high risk of bias when any one or more key domains are valued high. Otherwise, trials were rated to be unclear risk of bias. Disagreements were resolved following discussion with a third author (FJM).

Statistical analysis

We calculated risk ratio (RR) and mean difference (MD) to express the dichotomous and continuous data respectively. The 95% confidence interval (CI), corresponding to each effect size, was calculated to assess the precision of estimating pooled results. Heterogeneity across included studies was evaluated qualitatively using the Chi square method, and the I^2 statistic was used to quantify the level of heterogeneity. $I^2 \geq 50\%$ indicates significant heterogeneity. We selected random-effects model to perform meta-analysis if significant heterogeneity was detected, otherwise a fixed-effects model was used.

Quality of evidence

We assessed the quality of the evidence by using the GRADE approach (Balshem et al., 2011), in which the quality of a body of evidence underpinning an effect estimate represents confidence that the estimate is close to the quantity of specific interest (e.g., the effect of an intervention in the population of interest) (Grant et al., 2016). Briefly, the GRADE approach considers factors including risk of bias; inconsistency; indirectness; imprecision; and publication bias when judging the quality of evidence. Grades of evidence were as follows: High quality: Further research is very unlikely to change our confidence in the estimate of effect. Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality: We are very uncertain about the estimate.

Results

Study selection and basic characteristics

The identification and selection process of studies was depicted in Figure 1, and the basic characteristics of all eligible RCTs were summarized in Table 1. We identified initially 575 citations after searching all target electronic databases, and no trail was added through other sources. After deleted duplicate records and removed ineligible studies, a total of 8 RCTs comprising 1482 participants were eligible for our inclusion criteria.

Table.1 Characteristics of Included Trials

Study ID	No. of participants		Randomization	Age ,year (T/C)	Diseases	Intervention	Control	Outcomes
	Female	Male						
Ding et al 2014	68	70	Unclear	55.21±12.75 /54.51±12.53	Cancer	Continuous slow saline injection during catheter advancement	Head rotation to the side of cannulation	Malposition rate, Insertion time, Comfort level
Jia et al 2015	145	115	Sequential method	56.2±6.3	Cancer	Continuous slow saline injection during catheter advancement	Head rotation to the side of cannulation	Malposition rate, Insertion time, Comfort level
Lu et al 2010	37	63	Unclear	54.1/53.15	Cancer	Withdrawing guide wire ahead while sending	Head rotation to the side of cannulation	Malposition rate
Lu et al 2015	76	104	Unclear	43.5	Cancer	Withdrawing guide wire ahead while sending	Head rotation to the side of cannulation	Malposition rate, Complications rate
Wang et al 2010	117	70	Chronological order	54.96±16.63 /52.62±12.93	Parenteral nutrition	Continuous slow saline injection during catheter advancement	Head rotation to the side of cannulation	Malposition rate

Continued Table.1

Study ID	No. of participants		Randomization	Age ,year (T/C)	Diseases	Intervention	Control	Outcomes
	Female	Male						
Wang et al 2015	56	99	Unclear	56.6	Cancer	Continuous slow Saline injection during catheter advancement	Head rotation to The side of cannulation	Malposition rate
Wang et al 2015	395	5	Random number table	56/57	Breast cancer	Withdrawing guide wire ahead while sending	Head rotation to the side of cannulation	Malposition rate
Zhang et al 2016	92	107	Admission order	52±3.2	Homeopathy	Withdrawing guide wire ahead while sending	Head rotation to the side of cannulation	Malposition rate

Table.2 Modified sending method compared to traditional sending method with insertion of PICC

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk **Control**	 Corresponding risk **Final**	**Relative effect (95% CI)**	**No of Participants (studies)**	**Quality of the evidence (GRADE)**
The rate of malposition	**Study population**		**RR 0.16** (0.1 to 0.26)	1482 (8 studies)	□□□⊖ **moderate**[1,2]
	142 per 1000	**23 per 1000** (14 to 37)			
	Moderate				
	119 per 1000	**19 per 1000** (12 to 31)			
The time of insertion		The mean time of insertion in the intervention groups was **3.45 lower** (3.86 to 3.03 lower)		398 (2 studies)	□□⊖⊖ **low**[1,2]
VAS		The mean vas in the intervention groups was **1.61 lower** (1.82 to 1.39 lower)		398 (2 studies)	□□⊖⊖ **low**[1,3]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on

the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] incomplete reporting of random sequence generation in most of studies included, Lack of blinding, Lack of allocation concealment
[2] -0.5Outcomes display heterogeneity,point estimates all show benefits
[3] use visual analogue scale represent comfort level indirectly

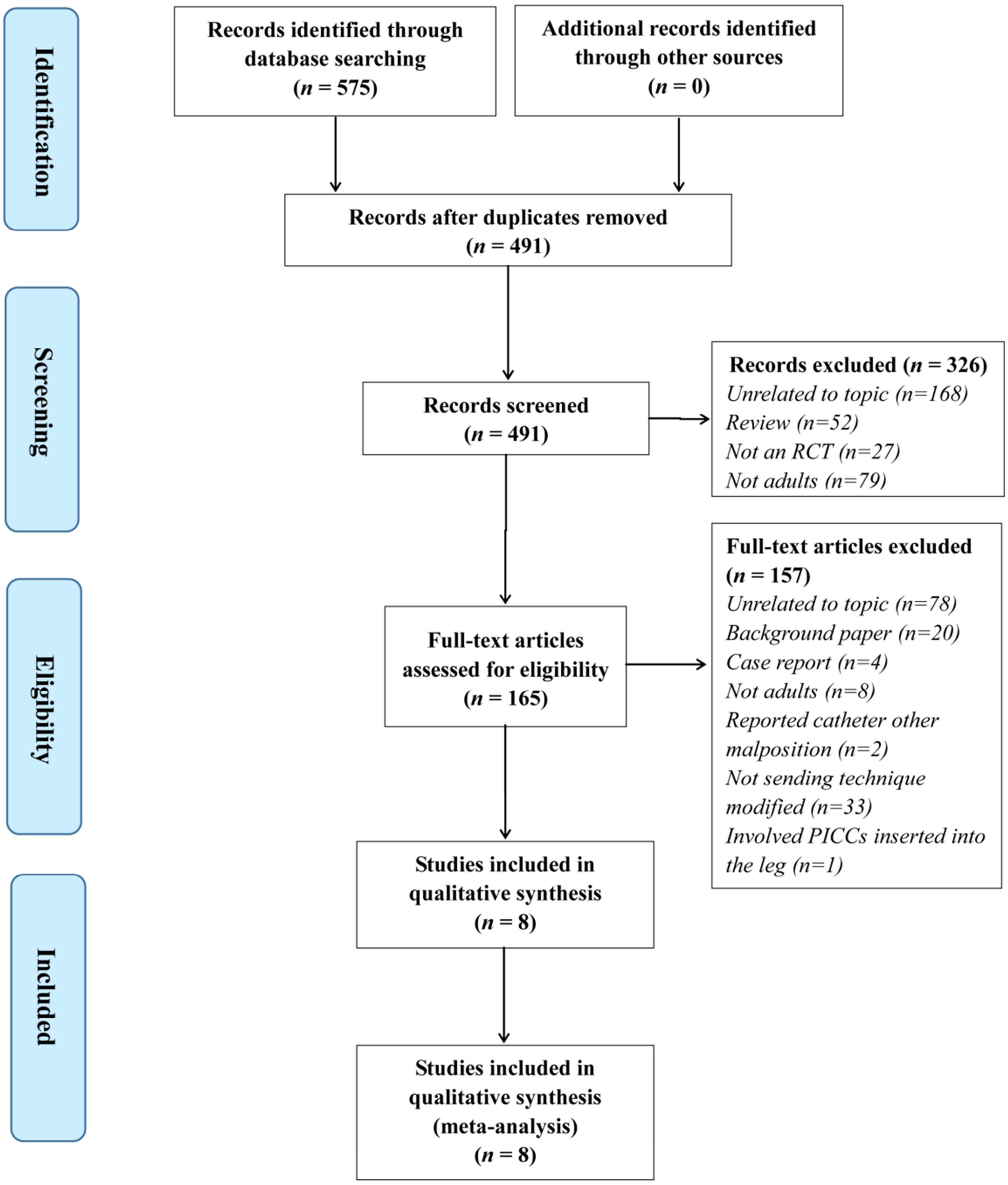
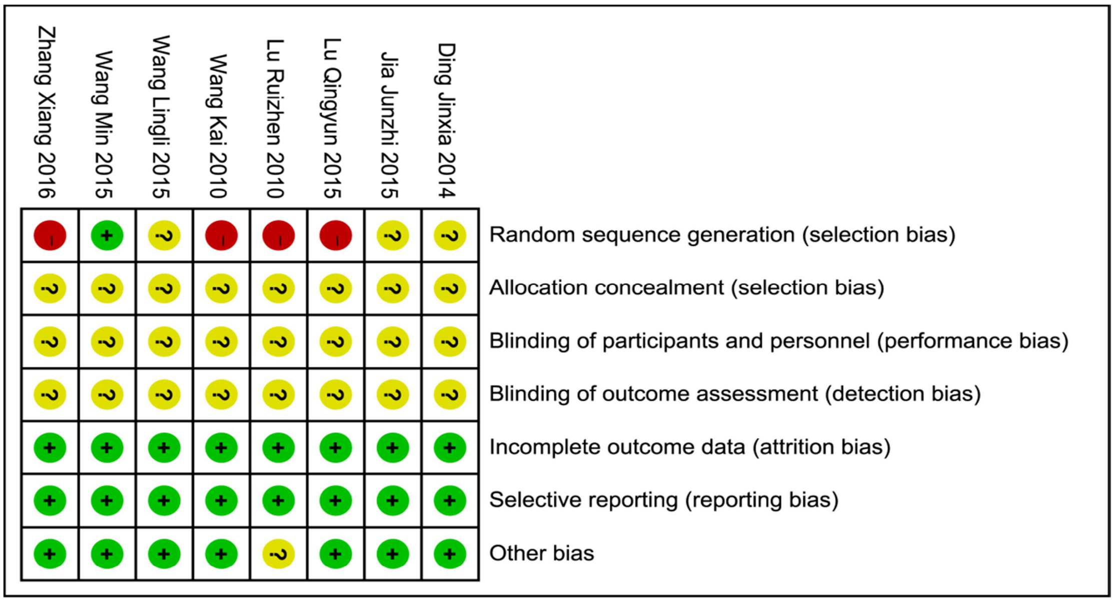
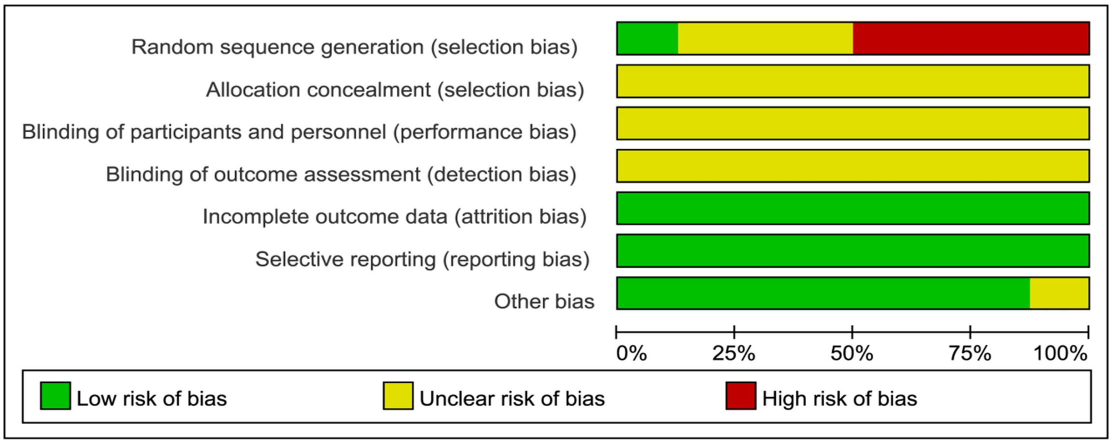


Figure.1 PRISMA Diagram chart of search and selection of literature. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analysis.



A. Risk of bias of each included studies



B. Summary of risk of bias of included studies

Figure.2 Assessment of risk of bias: (A) risk of bias of each included studies and (B) summary of risk of bias of included studies.

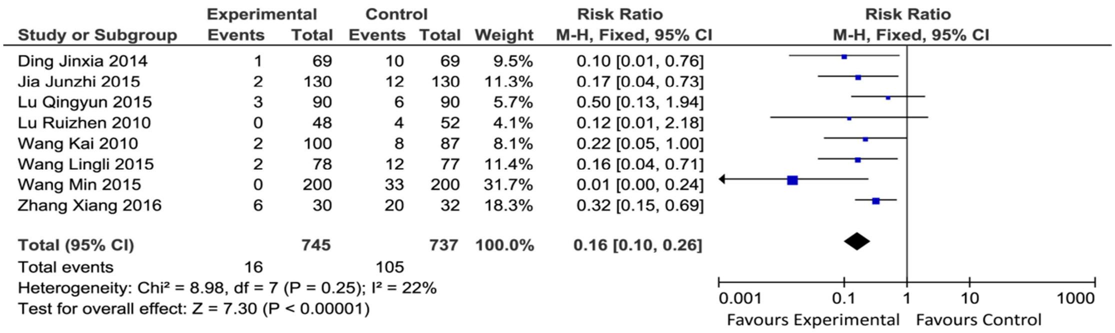


Figure.3 Meta-analysis on the rate of malposition: tip position cannot achieve an adequate position where the low superior vena cava or cavo-atrial junction is recommended, fixed-effect model.

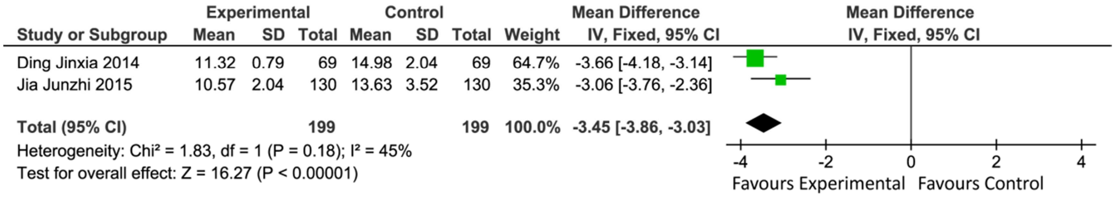


Figure.4 Meta-analysis on the time of insertion: the time of insertion has been slightly shortened after received the modified sending approach, fixed-effect model.

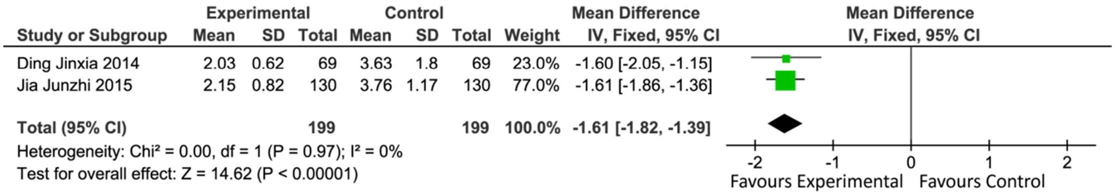


Figure.5 Meta-analysis the comfort level: the comfort level is measured by VAS indirectly, fixed-effect model. VAS = visual analogue scale.

Assessment of risk of bias

Details of risk of bias for each included trials were exhibited in Fig.2A and the summary of risk of bias of included studies in Fig. 2B. Most of the included studies have problems in blinding, concealment allocation and incomplete reporting of random sequence generat ion

Malposition rate

All of the trials (Ding et al., 2014, Jia, 2015, Lu et al., 2015, Lu, 2010, Wang et al., 2010, Wang and Wang, 2015, Wang et al., 2015, Zhang et al., 2016) involving 1482 participants reported the malposition rate. Significant heterogeneity was not detected (I^2 = 22%, P = 0.25), and thus we used fixed-effects model to calculate the effect size. Meta-analysis suggested that modified insertion technique was associated with a decreased risk of malposition during PICC (RR, 0.16, 95% CI, 0.10 to 0.26; $p < 0.001$) (see Figure 3).

Insertion time

Of all eligible RCTs, two (Ding et al., 2014, Jia, 2015), which enrolled 388 participants reported insertion time of interest. We did not detect significant heterogeneity (I^2 = 45%, P = 0.18). A fixed-effects model was therefore adopted to calculate effect size. Meta-analysis suggested that modified insertion technique was associated with shorter insertion time (MD, -3.45; 95% CI, -3.86 to -3.03; $p < 0.001$) (see Figure 4).

Comfort level

Two of all eligible trials (Ding et al., 2014, Jia, 2015), involving 388 patients, reported the comfort level, which was scored by using visual analogue scale (VAS). We did not detect statistical heterogeneity (I^2 = 0%, P = 0.97). We choose therefore fixed-effects model to calculate effect size. Meta-analysis suggested that modified insertion technique was associated with improved comfort level (MD, -1.61; 95% CI, -1.82 to -1.39; $p < 0.001$) (see Figure 5).

Discussion

In 1953, Dr. Sven Seldinger first described an over-wire technique for vessel cannulation (Zhang et al., 2016). While an improvement over previous approaches for accessing deep vessels, this technique entailed certain risks (Caparas et al., 2014). Present-day improvements to the original technique include the materials and design of the various components. Despite these improvements, the risk of malposition during PICC placement still remains.

The meta-analysis revealed that, compared with traditional sending method, modified technique effectively improves the accuracy of placing tip positioning. The success exploration of modified sending methods and optimization of corresponding operation process address the limitations traditional methods faced (such as, if patient is too weak to cooperate; patient may be so nervous that causing vasospasm). Withdrawing guide wire ahead method made the catheter forepart more flexible, with the 1000~1500ml/min speed of blood flow in subclavian vein, the tube could float to appropriate position (Wang et al., 2014). Continuous slow saline injection during catheter advancement could increase the front-end gravity which will lead tube to superior vena cava (Jia, 2015). Our meta-analysis suggested that modified sending method improves comfort level and shorten the time of insertion. However, the conclusion is still controversial with some drawbacks, such as insufficient allocation concealment, which may cause overestimating effect of intervention. And our meta-analysis has only searched English and Chinse databases, but not search for Korean, Japan or other databases, so there is a risk of incomplete retrieval. In addition, this study included only literature published in China, which affects the credibility of the pooled results of our meta-analysis. Owing to time goes by, techniques of PICC placement also improve; so it is needed to explore whether it is effective after about decade years.

To generate reasonable and reliable pooled results, we selected the GRADE approach to critically assess the evidence quality. Base on the GRADE evaluation criterion, the quality of evidence ranged from moderate to low for all outcomes. This was mainly due to risk of bias, inconsistency and indirectness within studies. If our confidence in the effect measure was downgraded, the reasons were mentioned in footnotes to the “summary of findings” table (Table 2).

Modified insertion techniques are beneficial for PICC placement, but it still has some questions for clinical promotion. For example, continuous slow saline injection method may not suite for patients restricted sodium intake. Modified techniques should be more standardized and systematic. As a result, more studies are needed in order to further explore a standard operation approach. In recent years, visible placement technique (e.g., 3CG TCS) are developed in west countries, but the cost for materials and equipment used in the PICC procedure is much higher than the procedure fee itself, causing a considerable economic burden for patients, particularly for those with poor economic status in China. In practice, modified sending methods (which belonging blind placement) may be less than optimal based on visible placement, but this simple intervention added no cost to the patient, used already available equipment, and conferred an additional minute to the duration of the initial procedure. So, we hope researchers do more studies to provide more standardized, scientific, rationalized approach for clinical use.

Conclusion

In conclusion, modified insertion techniques can effectively prevent the malposition during PICC insertion, shorten the time of insertion, and improve the comfort level, so it is worthy to be used widely in hospitals to improve the clinical outcomes of PICC placement. Manipulation of PICC with modified insertion techniques may further decrease the risk of vessel erosion and additional potential cost savings from avoiding second procedure of placement. While RCTs with largescale and high-quality based on RIS are warranted to further investigate the effectiveness of insertion techniques for PICC placement and may explore whether it has the potential for other variable on it.

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