Central Venous Catheterization (CVC) Site Choice Based on Anatomical Landmark Technique: A Systematic Review and Meta-analysis

Short title: CVC Site Choice Strategy

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Research

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Abstract

BACKGROUND: Internal jugular vein (IJV) and subclavian vein (SCV) have been the most preferred central venous catheterization (CVC) sites clinically. Based on individual preference and institutional routine, however, the choice of IJV catheterization (IJVC) or SCV catheterization (SCVC) is lack of high-level evidence. We sought to provide useful clinical strategy by comparing the catheterization time, success rate and the mechanical complications involved of the two CVCs.

METHODS: We systematically reviewed eligible studies from PubMed, OVID, Cochrane and ClinicalTrials.gov till February 2020. The primary outcomes were catheterization time and overall success rate, and the secondary outcomes were the first-attempt success rate and the instant mechanical complications.

RESULTS: A total of 3378 patients from 7 studies were included in the analysis. Neither difference was found on the catheterization time (SMD 95% CI: -0.095-0.124, $p=0.792$), nor any difference on the overall success rate (RR=1.017, 95% CI: 0.927-1.117, $p=0.721$, $I^2=89.6\%$) between the 2 procedures. However, subgroup analysis showed overall success rate of IJVC was significantly lower than that of SCVC (RR=0.906, 95%CI:0.850-0.965, $p=0.002$) in adult patients. The first-attempt success rate of IJVC group was higher than SCVC group in the adult patients (RR=1.472, 95%CI:1.004-2.156, $p=0.047$). No significance was detected in arterial injury (RR=1.137, 95% CI: 0.541-2.387, $p=0.735$) and pneumothorax (RR=0.600, 95% CI: 0.32-1.126, $p=0.112$) between the two procedures. Hematoma was significantly more in IJVC group than that in SCVC group (RR=2.824, 95% CI: 1.181-6.751, $p=0.02$).

CONCLUSIONS: Compared with IJVC, SCVC has a higher overall success rate while a lower first-attempt success rate in adults, and has involved with less hematoma. However, more high-quality studies are essential to provide better evidence especially in pediatric patients.

TRIAL REGISTRATION: This meta-analysis was pre-registered in PROSPERO (CRD42020165444).

Introduction

Subclavian vein (SCV) and internal jugular vein (IJV) catheterizations were first described in the 1950s and 1960s¹. Since then, various studies have shown other routes to the central venous system. Still, the internal jugular vein catheterization (IJVC) and subclavian vein catheterization (SCVC) are the most preferable ways for fluid and medication therapy, transfusion, blood volume monitoring, and parenteral nutrition².

However useful it is, the central venous catheterization (CVC) itself and associated adverse events shouldn't be neglected. The longer time took in CVC, the more discomforts the patients will experience³, and a higher insertion success rate correlates with lower mechanical complications⁴, which are expensive to treat and hazardous to patients². Most of the CVC practice choice is currently based on the experience and institutional routine that are lack of high-level evidence. Besides, since the ultrasound assisted catheterization was introduced into clinics, doctors tend to resort to ultrasound assistance when confronted by difficult catheterizations³, which seemingly dwarfs the traditional landmark method. Yet, no definitive evidence has shown its superiority over traditional anatomical ways in decreasing catheterization time, complications and cannulation failure, let alone the essential training, personnel and budget⁵⁻⁹. In fact, the landmark-based anatomical CVCs are overwhelmingly used in the less developed countries compared to ultrasound assistance¹⁰. Hence, whether ultrasound technique should be widely used among all kinds of patients and all CVCs is still uncertain^{2,7,11,12}. Plus, perioperative management of CVC counts not only on the most frequent instant complications that include arterial injury, pneumothorax and hematoma^{2,13}, also on the success rate and time when efficiency matters a lot.

So far, no guidelines or high levels of evidence concerning the choice of IJVC or SCVC have been published. Therefore, we conducted this systematic review and meta-analysis, comparing the landmark-based catheterization time and the success rate, as well as the instant mechanical complications between IJVC and SCVC, hoping to provide useful strategy for CVC management.

Methods

Search strategy

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations during the preparation of this review. And the protocol was registered with PROSPERO (registration no. CRD42020165444). Eligible studies were searched from the inception to February 2020 in PubMed, OVID, Cochrane and ClinicalTrials.gov, with key words "internal jugular

vein/venous", "subclavian vein/venous", "central venous catheterization", "central venous cannulation", "central venous insertion", "central line catheterization/cannulation/insertion". Potentially eligible studies were also manually searched from the references in the included studies. The limits to these searches were clinical trials, English language and humans.

Inclusion and exclusion criteria

All randomized controlled trials (RCTs) and non-randomized prospective cohort studies (PCs) that compared the two primary outcomes (catheterization time, overall success rate) or the secondary outcomes (first-attempt success rate, arterial injury, pneumothorax, hematoma) based on landmark technique between IJVC and SCVC were included. If a study included more than IJVC and SCVC, only the data of IJVC and SCVC were included, and if only one of the two procedure was involved, it was excluded. Case reports, review articles and editorials were excluded. If ultrasound technique was resorted to after a failed landmark-based catheterization, it was considered a failure, and if used under any circumstances, it would be excluded.

Data collection

Qualified studies were included by the consensus of two authors (WTX and QQZ), if disagreement occurred, the third author (XL) was asked to make the final decision. Data extraction from the qualified studies was carried out by two authors (ZGC and DF) in duplicate, a team discussion would be performed and final decision made in case of discrepancies. Data regarding the first author, published year, demographics of the patients, technique used (with or without ultrasound assistance), research type, overall sample size, number of patients in each study arm, catheter lumen, the catheterization mean time and standard deviation (SD), the first-attempt success, the overall success, the failures, and the incidents of arterial injury, pneumothorax and hematoma were all recorded in EXCEL 2010. Original authors were contacted if associated data was ambiguous or missed. The data information about the authors, magazines, publication years was concealed for later evaluations.

The primary outcomes were the catheterization time and overall success rate. The catheterization time was defined as the time spent from the start of the skin preparation till the catheter was inserted in the right place, recorded as mean time $\pm$ SD. The overall success rate was successful catheterizations among all participants in one group. Successful CVC was defined as the cannulation was achieved within three attempts by landmark technique¹⁴. The secondary outcomes were the first-attempt success rate and the incidents of arterial injury, pneumothorax and hematoma. The first-attempt success rate was defined as the catheter syringe penetrated into the aimed vein and successfully catheterized during the first try among all the patients in a group.

Risk of bias assessment

Our primary intention was to extract data from randomized trials, but only 3 studies were qualified. Hence, we made a group discussion and included non-randomized studies too. For randomized studies, the qualities were independently assessed by JW and XHJ using The Cochrane Collaboration's tool¹⁵. Six domains were included: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting and other bias. A score was assigned to each domain by consensus. The risk of bias in each RCT was ranked as low (over 5 domains with "yes"), moderate (3 or 4 domains with "yes"), and high (less than 2 domains with "yes")¹⁶(Table 1).

For non-randomized studies, the qualities were evaluated by HPZ and JS independently with the Newcastle-Ottawa scale¹⁷ (Table 2). Three main domains were included: patient selection, comparability and outcome assessment. The quality score of each study was summed, and the study was considered to be of high quality if the score was over 7 points¹⁶. The corresponding author would be consulted and made the final decision if disagreement occurred during these evaluations.

Statistical analysis

Most of the data were extracted and calculated from the manuscript. If the data required were not in the manuscript, we tried to contact the corresponding authors. Continuous data in this review was the catheterization time that was recorded as mean $\pm$ SD. The dichotomous data included the overall success rate, first-attempt success rate and the mechanical complications (arterial injury, pneumothorax and hematoma). Heterogeneity of the outcomes was reported using I^2 statistics (>75% indicating high heterogeneity, 25%-50% indicating moderate heterogeneity and <25% indicating low heterogeneity)¹⁸. Since age has been an important variable in catheterizations, we would set age as an indicator for subgroup analysis. The funnel plot was used to examine the risk of publication bias in the outcomes¹⁹. All of the analyses were performed using STATA 12.0 (Stata Corp LP, College Station, USA). Two-sided of alpha 0.05 was used for all statistics.

Results

In total, 1554 records were found and screened, 43 were extracted after title screening. Among which, 36 articles were excluded because of intervention or article types. And only 7 studies^{4, 13, 14, 20-23} were included in the qualitative and quantitative synthesis (**Figure 1**). A total of 4520 patients were included in the seven studies. However, 962 patients in IJVC group and 180 patients in SCVC group were dropped out, because ultrasound guidance was taken since the first attempt. Finally, 1783 and 1595 patients were analyzed in each group. For studies that included more than just IJVC and SCVC^{4, 13, 22, 23}, we extracted data only related to IJVC and SCVC. The details of the included studies are summarized in **Table 3**.

Primary Outcomes

Catheterization time

Only two studies^{13, 14} recorded the catheterization time that was not their original established outcome, though, the meta-analysis showed no difference in catheterization time between IJVC and SCVC (SMD 95% CI: -0.095-0.124, $p=0.792$, **Figure 2**). The operators and the patients in the two studies significantly varied (**Table 3**) that were complicated doctors (experienced and non-experienced) to adults¹³ and experienced doctors to children (<6 y)¹⁴. Low heterogeneity ($I^2=0.0\%$) was detected; however, the clinical heterogeneity could've played a key role in this comparison. The inconsistent and limited studies we retrieved precluded us from any meaningful conclusion between the two procedures. More high-quality randomized clinical trials focusing on the catheterization time would be essential to clarify this issue.

Overall success rate

Five studies^{4, 13, 14, 20, 22} compared the overall success rate were included in the quantitative analysis. No significance was detected in meta-analysis (RR=1.017, 95% CI: 0.927-1.117, $p=0.721$, **Figure 2**). This primary outcome was characterized by significant heterogeneity ($I^2=89.6\%$). Subgroup analysis based on age (18y) was performed. The subgroup analysis showed that the overall success rate of IJVC was significantly lower than that of SCVC (RR=0.906, 95%CI:0.850-0.965, $p=0.002$, **Figure 3**) in adult patient group. It's noteworthy that all catheterizations were finally achieved in a small sample size ($n=45$) study²¹ and it was excluded from the quantitative analysis. However, the pediatric patients group still posed high heterogeneity ($I^2=91.2\%$), two studies favored the IJVC for higher success rate^{20, 22} while the other two favored SCVC^{4, 14}.

Secondary Outcomes

First-attempt success rate

Only two studies^{14, 21} contributed to this secondary outcome, however, the heterogeneity was significant ($I^2=78.4\%$). Operated both by experienced doctors, the main differences lie in the age of patients and the catheter lumen (**Table 3**), for patients under 6 years old¹⁴, SCVC tended to achieve higher first-attempt success rate (**Figure 3**); while for adults²¹, IJVC had a significant higher first-attempt success rate that was contrary to the overall success rate (**Figure 3**).

Arterial injury

All the included studies recorded arterial injury complication, probably because it's one of the most common instant mechanical complications both in traditional landmark cannulation and the ultrasound assisted cannulation^{2, 24}. The seven studies together created a moderate heterogeneity ($I^2=70.2\%$), but no significant statistical difference was detected between the two insertion sites in the quantitative analysis (RR=1.137, 95% CI: 0.541-2.387, $p=0.735$, **Figure 2**).

Pneumothorax

Pneumothorax was evaluated in four studies^{4, 13, 14, 22}. The incidence of pneumothorax in IJVC group wasn't significantly different with that of SCVC group (RR=0.600, 95% CI: 0.32-1.126, $p=0.112$, $I^2=0.0\%$, **Figure 2**). Notably, three studies^{4, 13, 22} had a tendency indicating a lower incidence rate of pneumothorax in IJVC group.

Hematoma

The same four studies that evaluated pneumothorax also evaluated hematoma. Hematoma was significantly more in IJVC group than that in SCVC group (RR=2.824, 95% CI: 1.181-6.751, $p=0.02$, $I^2=4.8\%$, **Figure 2**).

Subgroup analyses

We conducted subgroup analyses to investigate the influence of patients' age on all outcomes. For the catheterization time, neither adult patients were detected of any statistical difference between the two procedures (SMD=-0.005, 95%CI: -0.123-0.113, $p=0.929$), nor were any statistical difference in pediatric patients (SMD=0.141, 95%CI: -0.145-0.437, $p=0.349$). Since this result was only recorded but not pre-designated as their outcome in the original two studies, as one of our primary outcomes, it seemed embarrassing. For overall success rate, the subgroup analysis by age has shown a significant lower overall success rate in IJVC group than that in SCVC group in adult patients (RR=0.906, 95%CI:0.850-0.965, $p=0.002$, **Figure 3**), however, high heterogeneity was shown in pediatric patients ($I^2=91.2\%$) and no significant difference was detected (RR=1.056, 95%CI:0.931-1.198, $p=0.395$, **Figure 3**).

The first-attempt success rate, when analyzed in subgroups, IJVC group achieved a higher first-attempt success rate than SCVC group in the adult patients (RR=1.472, 95%CI:1.004-2.156, $p=0.047$, **Figure 3**), whereas in the pediatric patients, no significant difference was detected (RR=0.931, 95%CI:0.788-1.100, $p=0.399$, **Figure 3**). The subgroup analyses of arterial injury didn't detect any statistical differences neither in adult patient group (RR=2.767, 95%CI:0.729-10.511, $p=0.135$, **Figure 3**) nor in pediatric patient group (RR=0.940, 95%CI:0.406-2.177, $p=0.149$, **Figure 3**) between the two procedures. Likewise, the subgroup analyses of pneumothorax incidents didn't find any statistical differences in different age groups between the two CVC ways (**Figure 3**). The hematoma incidence rate, however, when analyzed by age subgroups, IJVC showed significant higher rate than SCVC in adult patient group (RR=7.235, 95%CI:1.534-33.919, $p=0.012$, **Figure 3**), whereas in the pediatric patients, IJVC posed a higher risk trend but no significance was found (RR=1.870, 95%CI:0.689-5.077, $p=0.219$, **Figure 3**).

Sensitivity analyses

We conducted sensitivity analyses with a fixed effects model alternatively. The outcome of the catheterization time and first-attempt success rate were also performed regardless of small number of studies. The results of sensitivity analyses were largely consistent with the primary analysis. (supplemental data)

Publication bias

The funnel plots for the outcomes of overall success rate, arterial injury, pneumothorax and hematoma were conducted. Publication bias on the catheterization time and first-attempt success were not calculated because of limited studies included. Since the number of included studies for any outcome is small, the funnel plot could have limited power to detect the bias. (supplemental data)

Discussion

Our meta-analysis of seven studies shows that neither catheterization time nor overall success rate was significantly different between IJVC and SCVC, but the overall success rate of IJVC was significantly lower than that of SCVC in adult patients under age subgroup analysis. To our knowledge, this is the first meta-analysis so far that raises the attention to catheterization time and overall success rate between IJVC and SCVC based on anatomical landmark.

However, we cannot draw any conclusion from the primary outcomes, because the catheterization time was only recorded but not pre-designated as outcomes in two RCTs that makes it less convincing. Less convincing as it is, catheterization time matters clinically. Perioperative critical and emergent situations sometimes demand fast central lines for monitoring and therapy^{25,26}. And the choice of traditional landmark CVC shouldn't be focused only on the complications²⁷, prolonged catheterization time could result in severe complications like cardiac arrest, sudden apnea²⁸. The shorter time spent in catheterization, the more time reserved for other medical care and the less discomforts the patients will experience³. The real clinical operational time in catheterization, however, differs greatly, in the include 2 studies, the mean time for IJVC in adults was 765 seconds¹³, while in pediatric patients in another study, it was only 187 seconds¹⁴. The existence of clinical heterogeneity like different patients, operators or even different procedures for catheterization does not make this outcome less valuable, instead, it calls for better training for improvement, and most of all, more high-quality randomized studies focusing on catheterization time are essential to elaborate this issue. The overall success rate has been mostly adopted as an

outcome in the comparison of ultrasound assisted CVC and landmark CVC^{7, 11, 29}, it's valuable in our comparison of different CVC approaching sites as well. The lower overall success rate of IJVC in adults may be explained by its anatomy variations^{30, 31}, including the bifurcations that occur at different sites of the internal jugular vein, the bicuspid on the right side of the internal and the tricuspid on the left side. Another explanation could be that IJVC assisted by ultrasound is most recommended and easier to grasp⁹, while for SCVC, the failures and the instant complications weren't be reduced by ultrasound technique^{12, 32}, the operators would be more inclined to resort to ultrasound guidance when confronted by difficult cannulations during IJVC.

Some other important findings emerged from our meta-analysis. First, as one of the secondary outcomes, IJVC had a significant higher first-attempt success rate than SCVC in adult patients, contrary to the overall success rate, which also implied more attempts could've happened in the SCVC group. The first-attempt success rate correlates not only with the catheterization time, also with the mechanical complications^{14, 33}. Each attempt increases the risk of complications after two attempts⁴. CVC may result in many complications that could be instant mechanical complications, infection, thrombosis and even cardiovascular events^{2, 3}. Infection and thrombosis are mainly ascribed to CVC maintenance, while the mechanical complications mostly occur during the catheterization². Second, compared to SCVC, the arterial injury and pneumothorax in IJVC were not significantly different neither in adult patients nor in pediatric patients. However, SCVC induced hematoma was significantly less than IJVC, unfortunately, the subgroup analysis showed that pediatric patients might not benefit from it. Those findings indicate that age could be a potential effect modifier, however, due to limited studies, the interpretation of these differences could be questionable. More high-quality and well-designed studies based on different ages will be needed to clarify the differences of the two CVCs.

There are some limitations in our meta-analysis. First, we anticipated including only RCTs, but found only three RCTs were qualified^{13, 14, 20}, what's more, none of them were consisted of all age groups and the study quality differed (Table 1). For the PCs included, earning a total score of at least 6, though, they were subject to selection bias, information bias and measurement bias³⁴. As is known that the strength of the results that can be drawn from a meta-analysis is dependent on the quality of the included studies, the outcomes in our meta-analysis could be confounded and should be treated with considerable caution.

Second, the definitions of the outcomes that used in the studies were not unified. For example, the catheterization time and failure were not strictly defined in the largest RCT since they were not the pre-setting outcomes¹³, while in another RCT, the catheterization failure was defined as three consecutive unsuccessful attempts at one site¹⁴.

Third, significant heterogeneity was detected among the studies. It might be understandable in the ages of the patients, however, other aspects like the different experience of the operators, different lumens that could've created more heterogeneity were not well-defined either (Table 3), thus, the subgroup analyses stratified by these two were not conducted.

Aside from these limitations, our meta-analysis brought the importance of cannulation sites based on landmark method to the light in CVCs, whereas overwhelming studies concluded the superiority of ultrasound technology in CVCs. We are not trying to devalue the significance of ultrasound in CVCs, especially in some difficult catheterizations. What we are trying to clarify is that anatomy and experience matter in both landmark and ultrasound assisted CVCs. Besides, it could be tricky when encountered with limited medical resources, short of personnel and less training in ultrasound technique. Further, it could be much beneficial when CVCs are done fast and clean during the perioperative period.

In conclusion, compared with SCVC, IJVC shows no difference in catheterization time and a significant lower overall success rate in adult patients. SCVC produces a lower first-attempt success rate but less hematoma in adult patients. The shortage of high-quality studies in our meta-analysis undermines our conclusions. But, whenever it's difficult to identify the landmarks of one CVC, another route should be considered². For better evidence in choosing CVC sites, more well-designed, randomized trials are required.

Abbreviations

IJV = internal jugular vein; **SCV** = subclavian vein; **CVC** = central venous catheterization; **IJVC** = internal jugular vein catheterization; **SCVC** = subclavian vein catheterization; **SMD** = standardized mean difference; **CI** = confidence interval; **RR** = risk ratio; **RCT** = randomized controlled trial; **PC** = prospective cohort study; **SD** = standard deviation; **PRISMA** = Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Declarations

- **Ethics approval and consent to participate**

This study was pre-registered with PROSPERO (CRD42020165444). No informed consent would be necessary for this meta-analysis

- **Consent for publication**

Not applicable

- **Availability of data and materials**

The datasets generated and/ or analyzed are available from the corresponding author upon reasonable request.

- **Competing interests**

None

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- **Authors' contributions**

All authors were involved in this meta-analysis and have approved the final manuscript

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Tables

Table 1. Cochrane evaluations of the included RCTs

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Risk of bias
Han, 2004	Yes	No	Yes	No	Yes	No	No	Moderate
Jean, 2015	Yes	Yes	Yes	No	Yes	Yes	Yes	Low
Aynur, 2016	Yes	Yes	No	Yes	Yes	No	No	Moderate

RCT stands for randomized controlled study.

Table 2 Newcastle evaluation for non-RCTs

Study	Selection			Comparability	Outcome			Quality score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow up long enough for the outcomes to occur	Adequacy of follow up of cohorts	
Adnan, 2005	1	1	1	1	1	1	1	8
Bulent, 2007	1	1	1	1	0	1	1	7
Wolfram, 2007	1	1	1	0	0	1	1	6
Rey, 2009	1	1	1	0	0	1	1	6

RCT stands for randomized controlled study.

Table 3. Baseline characteristics of the included studies.

Study	Country	Design	Age (year)	Lumen	IJVC	SCVC	Executor
Han, 2004	Korea	RCT	<1	NA	136	136	Complicated
Adnan, 2005	Turkey	PC	>18	NA	23	22	Experienced
Bulent, 2007	Turkey	PC	<18	1-3	84	119	Experienced
Wolfram, 2007	Germany	PC	>6	NA	729	339	Experienced
Rey, 2009	Spain	PC	<18	1-3	293	116	Complicated
Jean, 2015	France	RCT	>18	NA	429	776	Complicated
Aynur, 2016	Turkey	RCT	<6	2-3	89	87	Experienced

IJVC indicates internal jugular vein catheterization; SCVC indicates subclavian vein catheterization; RCT indicates randomized controlled study; PC indicates prospective cohort study; NA indicates not available.

Figures

Figure 1

PRISMA flow diagram of the search results, exclusions and inclusions. PRISMA indicates Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Figure 2

Pooled relative risk of catheterization time (A), overall success rate (B), first-attempt success rate (C), and instant mechanical complications including arterial injury (D), pneumothorax (E), and hematoma (F). IJVC = internal jugular vein catheterization; SCVC = subclavian vein catheterization; SMD = standardized mean difference; RR = relative risk; CI = confidence interval.

Figure 3

Subgroup analyses of catheterization time (A), overall success rate (B), first-attempt success rate (C), arterial injury (D), pneumothorax (E), and hematoma (F). IJVC = internal jugular vein catheterization; SCVC = subclavian vein catheterization; SMD = standardized mean difference; RR = relative risk; CI = confidence interval.

Supplementary Files

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