Intravenous Infusion Route in Maternal Resuscitation: A Scoping Review

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Abstract

**Background:** The upper extremities can be used as an infusion route during cardiopulmonary resuscitation in pregnant women. This is a reasonable recommendation considering the characteristic circulation of pregnant women, but this method is not based on scientific evidence.

**Objective** of the Review: We conducted a scoping review to determine whether the infusion route should be established above the diaphragm during cardiopulmonary resuscitation in a pregnant woman.

**Discussion:** We included randomized controlled trials (RCTs) and non-RCTs on the infusion of fluids in pregnant women after 20 weeks of gestation requiring establishment of an infusion route due to cardiac arrest, massive bleeding, intra-abdominal bleeding, cesarean section, severe infection, or thrombosis. In total, 3150 articles from electronic database were extracted, respectively. After title and abstract review, 265 articles were extracted, and 116 articles were extracted by full-text screening, which were included in the final analysis. The 116 articles included 78 studies on infusion for pregnant women. The location of the intravenous infusion route could be confirmed in only 17 studies, all of which used the upper extremity to secure the venous route.

**Conclusion:** Pregnant women undergo significant physiological changes that differ from those of normal adults, because of pressure and drainage of the inferior vena cava and pelvic veins by the enlarged uterus. Therefore, despite a lack of evidence, it seems logical to secure the infusion route above the diaphragm when resuscitating a pregnant woman.

Introduction

The Japan Resuscitation Council (JRC) has published resuscitation guidelines in 2010 and 2015, and in the 2020 revision, they plan to create an algorithm for resuscitation of pregnant women. Hence, we decided to create an algorithm for resuscitation of pregnant women as a special situation of cardiac arrest.

Although the number of maternal deaths in Japan is approximately 4 per 100,000 deliveries [1], which is a small number compared to that reported worldwide, it is important to create an evidence-based maternal resuscitation algorithm because there are potentially many pregnancy-related maternal cardiac arrests.

Therefore, we created a clinical question (CQ) from algorithm and 2015 statements of the American Heart Association (AHA). This report is a scoping review of an articles, “In cardiopulmonary resuscitation of pregnant women, should the infusion route be taken above the diaphragm for massive infusion?”

The AHA developed and illustrated an algorithm based on the International Consensus Conference on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations (CoSTR) [2], which stated that intravenous access should be considered above the diaphragm [3]. This statement makes sense considering the special circulatory dynamics of pregnancy,
but we believe that it needs to be supported by evidence and not by a scientific recommendation based on evidence. Therefore, we decided to conduct a comprehensive review of the maintenance of the infusion route in pregnant women. The purpose of this study was to scientifically support whether the infusion route should be secured above the diaphragm during maternal resuscitation by scoping review.

**Methods**

The maternal group within the JRC of the Guideline Editorial Committee established the CQ. However, since there are no valid studies on the location of the infusion route during resuscitation of pregnant women, we thought that systematic review would be difficult and decided to conduct a scoping review of all studies on the infusion route for pregnant women.

**Protocol and registration**

This study was systematized and conducted concerning the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) extension for Scoping Reviews checklist [4].

**Eligibility criteria**

Only articles published in peer-reviewed journals were included in the review, and those with abstracts only were excluded. Only literatures published in English were included, while articles published in other languages were excluded. Literatures on animals were excluded, and only studies on humans were included. The types of studies included were randomized control trials (RCTs), non-RCTs (such as split time-series analyses, before-and-after comparative studies, cohort studies, case reports, and meta-analyses), case-concentration studies, reviews, and existing guidelines. By contrast, unpublished studies (e.g., conference abstracts and clinical trial protocols) were excluded.

**Information sources**

Articles published on or before December 07, 2019 were retrieved from MEDLINE/PubMed and Embase. The search strategy was constructed by Marie Furuta, PhD Health Studies, an expert in public health (co-author of this paper).

**Search**

The search strategy is shown in Supplementary Material 1.

**Selection of sources of evidence**

Data charting of each literature was performed independently by two reviewers. In pairs sequentially evaluated the titles and abstracts, while screening of full-text articles were performed independently.

**Data charting process**
Population, concept, and context (PCC) frameworks were created [5], as shown in Table 1. The study was conducted in pregnant women who received fluid infusions after 20 weeks of gestation. As a Concept, RCTs and non-RCTs (split time-series analysis, before-and-after comparative studies, cohort studies, case reports, and meta-analysis) were included in studies of patients requiring intravenous infusion or intraosseous infusion due to cardiac arrest, massive bleeding, intra-abdominal hemorrhage, cesarean section, severe infection, and thrombosis. As a context, a literature search was performed, regardless of the region in which the study was conducted, race, or differences in healthcare systems by medical area. A data-charting form was jointly developed by two reviewers to determine the relevant articles that should be extracted.

| Table 1 |
|-------------------------|
| **PCC (Population, Concept, Context) frameworks** |

**Population:** A study on the infusion of fluids in pregnant women after 20 weeks of gestation.

**Concept:** RCT and non-RCT (split time-series analysis, before-and-after comparative studies, cohort studies, case reports, and meta-analysis) were included in studies of patients requiring intravenous infusion or intraosseous infusion due to cardiac arrest, massive bleeding, intra-abdominal hemorrhage, cesarean section, severe infection, and thrombosis.

**Context:** We searched the literature, regardless of the region in which the study was conducted, race, or differences in healthcare systems by medical area.

**Results**

**Selection of sources of evidence**

Figure 1 shows the PRISMA flowchart [6] for this scoping review.

**Characteristics of sources evidence**

The search for articles was performed on December 07, 2019 based on the search formula described above, and 1194 articles were extracted from MEDLINE/PubMed and 1956 articles were extracted from Embase. After title and abstract review, 265 articles met the eligibility criteria by deduplication and relevance screening. Supplementary Material 2 shows the list of references in which full text screening was conducted. Then, full-text screening was conducted, and 116 references were extracted for the final analysis.

**Results of individual sources of evidence**

Table 2 presents the details of the breakdown of the 116 articles.
Table 2
General characteristics of included articles.

| Study design          | Caesarean section (n = 78) | Postpartum bleeding (n = 11) | Maternal cardiac arrest (n = 7) | Other complications in pregnancy† (n = 20) |
|-----------------------|---------------------------|------------------------------|-------------------------------|------------------------------------------|
| RCT                   | 54                        | 5                            | 0                             | 6                                        |
| Prospective cohort study | 15                       | 0                            | 0                             | 2                                        |
| Retrospective cohort study | 0                        | 1                            | 1                             | 1                                        |
| Case control study    | 0                         | 0                            | 0                             | 0                                        |
| Cross sectional study | 0                         | 0                            | 0                             | 3                                        |
| Case control study    | 0                         | 0                            | 0                             | 0                                        |
| Case report and case series | 0                     | 0                            | 4                             | 0                                        |
| Meta analysis         | 3                         | 0                            | 0                             | 0                                        |
| other                 | 6                         | 5                            | 2                             | 8                                        |

† Reports on the infusion route, including infections, thrombosis, and administration of pressure-boosting drugs in pregnant women

The 116 articles included (1) 78 studies on the infusion of fluids during cesarean section in pregnant women (3 meta-analyses, 54 RCTs, 15 prospective cohort studies, and 6 others), (2) 11 studies on the infusion of fluids during hemorrhage in pregnant women (5 RCTs, 1 prospective cohort study, and 5 others) 5 RCTs, 1 backward cohort study, and 5 other studies; (3) 7 studies on the infusion of fluids during cardiac arrest in pregnant women (1 backward cohort study, 4 case reports, and 2 other studies); and (4) 20 studies on the infusion of fluids for infection, thrombosis, and other conditions in pregnant women (6 RCTs, 2 prospective cohort studies, 1 backward cohort study, 3 case reports, and 8 other studies). The location of the infusion route (upper or lower extremity) could be confirmed in only 17 studies, all of which used the upper extremity to secure the venous route. Table 3 shows a list of references that mention the infusion route.
Table 3

All references that mention the location of the infusion route

| Author          | Article type       | Published year | Population                                                                 | Location of the intravenous infusion route |
|-----------------|--------------------|----------------|---------------------------------------------------------------------------|-------------------------------------------|
| Pouta et al. (13) | Randomized controled trial | 1996          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| King et al. (14)  | Randomized controled trial | 1998          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Ngan et al. (15)  | Randomized controled trial | 2000          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Desalu et al. (16) | Randomized controled trial | 2005          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Ngan et al. (17)  | Randomized controled trial | 2005          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Ngan et al. (18)  | Randomized controled trial | 2008          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Nuthalapaty et al. (19) | Retrospective study | 2009          | Study on infusion for pregnant and postpartum patients                     | Upper extremities                         |
| Chatterjee et al. (20) | Case report       | 2011          | Massive obstetric haemorrhage                                              | Upper extremities                         |
| El-Mekawy et al. (21) | Randomized controled trial | 2012          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Romdhani et al. (22) | Randomized controled trial | 2014          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Cape et al. (23)  | Retrospective study | 2014          | Patients with peripherally inserted central catheter during pregnancy       | Upper extremities                         |
| Zasa et al. (24)  | Randomized controled trial | 2015          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Onwochei et al. (25) | Prospective study     | 2017          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
| Ngan et al. (26)  | Randomized controled trial | 2017          | Pregnant woman undergoing a cesarean section                              | Upper extremities                         |
We also conducted a comprehensive search for studies on maternal bone marrow tracts, but no relevant studies were identified. We also conducted a comprehensive search for studies on the maternal intraosseous infusion route, but no relevant studies were identified.

### Summary of evidence

As it was difficult to conduct a systematic review, a scoping review was performed. We found some literatures related to the infusion of fluids during surgery and bleeding in pregnant women, including RCTs, but did not find any valid studies related to the infusion route in pregnant women.

### Discussion

There are no RCTs on maternal infusion routes; therefore, a systematic review was not possible. This comprehensive scoping review revealed the number of studies mentioning the infusion route in detail is scarce, and the level of evidence for securing the infusion route above the diaphragm is considered small. However, there is no evidence of the adverse effects of securing the infusion route above the diaphragm. Furthermore, the AHA recommendations are supportive, considering the pressure drainage of the inferior vena cava caused by an enlarged uterus in pregnant and nursing women, as mentioned above.

In the 2010 AHA Guideline, Part 12: Cardiac arrest in special situations, it was recommended that the infusion route be secured above the diaphragm [2]. The AHA likely came to this view considering the following special circulatory dynamics of pregnant and nursing women. Significant physiological changes occur in pregnant and nursing women, which differ from those in normal adults. In addition to increasing circulating blood volume up to 50%, decreasing peripheral vascular resistance, and increasing in cardiac output, the enlarged uterus causes pressure drainage of the inferior vena cava and pelvic veins, resulting in partial venous hypertension and edema [7].

It makes sense to secure an infusion route above the diaphragm so that infusions and administered drugs can reach the heart without passing through the distended inferior vena cava [8], and the AHA...
recommendation seems reasonable considering the unique circulatory dynamics of pregnant and nursing women.

The problem is that these recommendations are reasonable based on the special circulatory dynamics of pregnant and nursing women, but they are not based on evidence from the literature. Although some studies have suggested that an infusion route below the diaphragm should be avoided because an enlarged uterus pressurizes and inhibits venous return [9], a high-quality RCT of infusion routes during maternal resuscitation seems impossible due to the ethical difficulties of randomization and blinding.

In non-pregnant women, there were three observational studies of adult out-of-hospital cardiac arrest with a total of 34,868 patients comparing the upper and lower extremity infusion routes [10–12]. Compared to the use of the venous route in the upper extremities, the use of the bone marrow route in the lower extremities was associated with worse outcomes such as poor survival, with < 17 patients discharged alive per 1,000 cardiac arrest patients. Thus, although indirect, it is possible that the outcome of cardiac arrest may be better if the infusion route is secured through the upper arm.

**Conclusion**

Pregnant women undergo significant physiological changes that differ from those of normal adults, because of pressure and drainage of the inferior vena cava and pelvic veins by the enlarged uterus. Therefore, despite a lack of evidence, it seems logical to secure the infusion route above the diaphragm when resuscitating a pregnant woman.

**Declarations**

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interest.

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**Author contributions**
EN, ST, SM, HT, and AS are conceived the study design.

Methodology are constructed by MF and AS.

Formal analysis and investigation were performed by EN, ST, and MF.

Review and editing were performed by EN and ST.

All authors read and approved the final manuscript.

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References

1. Hasegawa J, Sekizawa A, Tanaka H, et al. Current Status of Pregnancy-related Maternal Mortality in Japan: A Report from the Maternal Death Exploratory Committee in Japan. BMJ Open 2016;6:e010304.

2. Vanden Hoek TL, Morrison LJ, Shuster M, et al. Part 12: Cardiac Arrest in Special Situations: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122:S829-S861.

3. Jeejeebhoy FM, Zelop CM, Lipman S, et al. Cardiac Arrest in Pregnancy: A Scientific Statement From the American Heart Association. Circulation 2015;132:1747–1773.

4. Tricco AC, Lillie E, Zarin W, O'Brien KK, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Int Med 2018;169:467–473.

5. Institute JB. Joanna Briggs Institute Reviewers' Manual 2015: Methodology for JBI Scoping Reviews. 2015.

6. Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-analyses: The PRISMA statement. PLoS Med. 2009;6:e1000097.

7. Hill CC, Pickinpaugh J. Physiologic Changes in Pregnancy. Surg Clin North Am 2008;88:391–401.

8. Hofmeyr GJ. Prophylactic Intravenous Preloading for Regional Analgesia in Labour. The Cochrane Database of Systematic Reviews. 2002:Cd000175.

9. Crochetière C. Obstetric Emergencies. Anesthesiology Clinics of North America. 2003;21:111–25.

10. Feinstein BA, Stubbs BA, Rea T, et al. Intraosseous compared to intravenous drug resuscitation in out-of-hospital cardiac arrest. Resuscitation 2017;117:91–96.

11. Kawano T, Grunau B, Scheuermeyer FX, et al. Intraosseous Vascular Access Is Associated With Lower Survival and Neurologic Recovery Among Patients With Out-of-Hospital Cardiac Arrest. Ann Emerg Med 2018;71:588–96.
12. Mody P, Brown SP, Kudenchuk PJ, et al. Intraosseous versus Intravenous Access in Patients with Out-of-hospital Cardiac Arrest: Insights from the Resuscitation Outcomes Consortium Continuous Chest Compression Trial. Resuscitation 2019;134:69–75.

13. Pouta AM, Karinen J, Vuolteenaho OJ, et al. Effect of Intravenous Fluid Preload on Vasoactive Peptide Secretion during Caesarean Section under Spinal Anaesthesia. Anaesthesia 1996;51:128–132.

14. King SW, Rosen MA. Prophylactic Ephedrine and Hypotension Associated with Spinal Anesthesia for Cesarean Delivery. Int J Obstet Anesth 1998;7:18–22.

15. Ngan Kee WD, Khaw KS, Lee BB, et al. A Dose-response Study of Prophylactic Intravenous Ephedrine for the Prevention of Hypotension during Spinal Anesthesia for Cesarean Delivery. Anesth Analg 2000;90:1390–1395.

16. Desalu I, Kushimo OT. Is Ephedrine Infusion More Effective at Preventing Hypotension than Traditional Prehydration during Spinal Anaesthesia for Caesarean Section in African Parturients? Int J Obstet Anesth 2005;14:294–299.

17. Ngan Kee WD, Khaw KS, Ng FF. Prevention of Hypotension during Spinal Anesthesia for Cesarean Delivery: An Effective Technique using Combination Phenylephrine Infusion and Crystalloid Cohydration. Anesthesiology 2005;103:744–750.

18. Ngan Kee WD, Lee A, Khaw KS, et al. A Randomized Double-blinded Comparison of Phenylephrine and Ephedrine Infusion Combinations to Maintain Blood Pressure during Spinal Anesthesia for Cesarean Delivery: The Effects on Fetal Acid-Base Status and Hemodynamic Control. Anesth Analg 2008;107:1295–1302.

19. Nuthalapaty FS, Beck MM, Mabie WC. Complications of Central Venous Catheters during Pregnancy and Postpartum: A Case Series. Am J Obstetr Gynecol 2009;201:311.e1-5.

20. Chatterjee DJ, Bukunola B, Samuels TL, et al. Resuscitation in Massive Obstetric Haemorrhage using an Intraosseous Needle. Anaesthesia 2011;66:306–310.

21. El-Mekawy NM. Comparative Study between Ephedrine Infusion vs. CO/Post Loading of Fluids for Prevention of Hypotension in Emergency Cesarean Section under Spinal Anesthesia. Egypt J Anaesth 2012;28:193–198.

22. Romdhani C, Trabelsi W, Lebbi A, et al. Lower Incidence of Hypotension Following Spinal Anaesthesia with 6% Hydroxyethyl Starch Preload Compared to 9‰ Saline Solution in Cesarean Delivery. Tunis Med 2014;92:406–410.

23. Cape AV, Mogensen KM, Robinson MK, et al. Peripherally Inserted Central Catheter (PICC) Complications during Pregnancy. JPEN J Parenter Enteral Nutr 2014;38:595–601.

24. Zasa M, Conci E, Marchignoli A, et al. Comparison of Two Different Approaches to Hypotension Following Spinal Anaesthesia for Caesarean Delivery: Effects on Neonatal and Maternal Wellbeing. Acta Biomed 2015;86:45–52.

25. Onwochei DN, Ngan Kee WD, Fung L, et al. Norepinephrine Intermittent Intravenous Boluses to Prevent Hypotension During Spinal Anesthesia for Cesarean Delivery: A Sequential Allocation Dose-
26. Ngan Kee WD, Tam YH, Khaw KS, et al. Closed-Loop Feedback Computer-Controlled Phenylephrine for Maintenance of Blood Pressure During Spinal Anesthesia for Cesarean Delivery: A Randomized Trial Comparing Automated Boluses Versus Infusion. Anesth Analg 2017;125:117–123.

27. Ngan Kee WD. A Random-allocation Graded Dose-Response Study of Norepinephrine and Phenylephrine for Treating Hypotension during Spinal Anesthesia for Cesarean Delivery. Anesthesiology 2017;127:934–941.

28. Ngan Kee WD, Lee SWY, Ng FF, et al. Prophylactic Norepinephrine Infusion for Preventing Hypotension During Spinal Anesthesia for Cesarean Delivery. Anesth Analg 2018;126:1989–1994.

29. Webster J, Larsen E, Booker C, et al. Prophylactic Insertion of Large Bore Peripheral Intravenous Catheters in Maternity Patients for Postpartum Haemorrhage: A Cohort Study. Aust N Z J Obstet Gynaecol 2018;58:548–552.

Figures

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