Original Article

Obstet Gynecol Sci 2020;63(5):605-614
https://doi.org/10.5468/ogs.20080
pISSN 2287-8572 · eISSN 2287-8580

Obstetrics & Gynecology Science

Perspective of the comparative effectiveness of non-pharmacologic managements on postpartum hemorrhage using a network meta-analysis

Kyung Ju Lee, MD, PhD, DPH[1,2,*], Kwan Hong, MD[3,4,*], Hari Hwang, BS[1,3], Hijeong Choi, PhD[5], Sangho Sohn, MD, PhD[1]

[1]Department of Public Health, Korea University Graduate School, Departments of [2]Obstetrics and Gynecology, [3]Preventive Medicine, Korea University College of Medicine, [4]Department of Epidemiology and Health Informatics, Graduate School of Public Health, Korea University, Seoul, [5]Graduate School of Integrative Medicine, CHA University, Pocheon, Korea

Objective

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality worldwide and is both unpredictable and inevitable. While uterotonic drugs are routinely recommended, there is ongoing debate on the ideal intervention to control uterine bleeding. This review aims to compare the use of non-pharmacologic treatments with peripartum hysterectomy in cases of life-threatening uncontrolled obstetric hemorrhage. The review's objective is to use a network meta-analysis to help prevent maternal deaths and rank the treatments according to success rates.

Methods

We searched MEDLINE (PubMed), Embase, and the Cochrane Library, from January 2014 until December 2018. A second search was carried out in April 2019 before the final data analysis. Network meta-analysis allows for the calculation of the effect size between treatment groups through indirect treatment comparison.

Results

We confirmed that balloon-assisted management is the best intervention for uncontrolled postpartum bleeding with pharmacologic treatment. This is followed by uterine artery embolization and surgical procedures, which can help avoid the need for a hysterectomy. The balloon tamponade demonstrated lower failure rate than the surgical procedure with odds ratio (OR) of 0.44 and 95% confidence intervals (CIs) 0.50–30.54. Uterine artery embolization had a lower risk for hysterectomy than the surgical procedure group (OR, 0.74; 95% CI, 0.22–2.50).

Conclusion

For the quick treatment of postpartum bleeding, balloon tamponade is the best method for uncontrolled postpartum bleeding with pharmacologic treatment, followed by uterine artery embolization and surgical procedures.

Keywords: Postpartum hemorrhage; Balloon tamponade; Uterine artery embolization; Network meta-analysis

Introduction

Maternal and perinatal mortalities are surrogate measures of national health status and indicators of social development. In 2015, 303,000 women, around 830 women per day, were estimated to have died due to pregnancy- or childbirth-related complications worldwide. Fortunately, the global maternal mortality rate has been decreasing, with an annual continuous reduction rate of 2.3% [1]. Similarly, the maternal mortality ratio in Korea decreased from 14 deaths per 100,000

Received: 2020.03.26. Revised: 2020.05.10. Accepted: 2020.05.25.
Corresponding author: Kyung Ju Lee, MD, PhD, DPH
Department of Public Health, Korea University Graduate School, 73 Goryeodae-ro, Seongbuk-gu, Seoul 02841, Korea
E-mail: drlkj52551@korea.ac.kr
https://orcid.org/0000-0003-4655-1521

*These authors contributed equally to this work.

live births in 2005 to 8.4 in 2016 [2].

Worldwide, blood loss after birth contributed to nearly a quarter of all maternal mortality cases, with the most common cause of postpartum hemorrhage (PPH) being uterine atony, the failure of the uterus to contract after birth. Maternal morbidity due to uterine atony is far more common than any other causes of bleeding, such as placental abruption, placenta accreta, placenta previa, or peripartum hysterectomy [1,3-6].

More than one third to half of maternal mortality cases are reported within the first 24 hours after giving birth [1,3]. Furthermore, while the risk factors for severe hemorrhage have been identified, such hemorrhages continue to be unpredictable and inevitable. Active management of the third stage of labor, which involves administration of uterotonic drugs, early clamping of the umbilical cord, and controlled cord traction, has become standardized nationwide [7-9]. Routine administration of uterotonic agents during the third stage of labor is a key intervention and the most effective at preventing PPH due to uncertain causes [7,8].

In 2009, the World Health Organization (WHO) working group defined "maternal near-miss morbidity" as a life-threatening obstetric hemorrhage that requires urgent medical attention to prevent the death of the mother [10]. Near-miss events are used to monitor the quality of maternal health care and provide rapid and useful feedback to improve obstetric care. The non-pharmacological procedure to treat obstetric hemorrhage is stressful and surgically challenging, inevitably causing additional maternal morbidity and, occasionally, infertility.

Even though the risk factors for uterine atony have been identified, up to half of women with uterine atony after cesarean delivery had no risk factors [6]. It has been established that a prolonged third stage of labor increases the frequency of PPH [9]. However, active management with uterotonic agents and controlling the umbilical cord have been shown to decrease PPH by decreasing the duration of the third stage of labor [9]. The active and expectant management of obstetric hemorrhage were updated as part of postpartum management, and despite very low quality evidence, active management has been introduced in low income countries to reduce hemorrhage [8].

In cases of unresponsive bleeding in which uterotonic agents have been administered, non-surgical treatments, such as balloon tamponade or embolization, should be immediately or simultaneously applied [11-14]. If the bleeding worsens, surgical procedures such as uterine compression suture, pelvic vessel ligation, and hysterectomy are performed [15-17]. In clinical practice, however, there is still uncertainty about whether to perform non-surgical and/or surgical procedures after uncontrolled bleeding with pharmacological managements. Due of the lack of certainty, and the small number of studies published, it is essential to assess the impact of these forms of care on both the mother and the baby. Effective prevention of PPH, and appropriate intervention during PPH, are key in decreasing maternal mortality.

Therefore, this study aimed to use a network meta-analysis to compare the effect of non-pharmacologic managements versus peripartum hysterectomy on uncontrolled bleeding in cases of life-threatening obstetric hemorrhage. This review will help prevent maternal deaths by ranking different treatments according to effectiveness.

Materials and methods

This network meta-analysis was conducted according to the guideline of the PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations [18].

1. Search strategy

We searched MEDLINE (PubMed), Embase, and Cochrane Library from January 2014 to April 2019. Only studies in English were retrieved. The search terms used were: "(postpartum hemorrhage OR obstetric hemorrhage) AND (uterine packing OR balloon tamponade OR balloon occlusion OR brace suture OR vessel ligation OR Blakemore tube OR Bakri OR B-lynch OR square suture OR uterine artery ligation OR internal iliac artery ligation OR uterine artery embolization)", using both MeSH terms and text words.

2. Inclusion and exclusion criteria

The following study types were included: randomized controlled trials (RCT), observational studies, and controlled trials (non-RCT/CT), all written in English. We excluded studies with case series or studies that only published an abstract. Participants included women in the third stage of labor who had a vaginal or cesarean birth in a hospital or a community setting. In electronic medical records, eligible patients were

PPH patients with at least 500 mL of blood loss at delivery and/or at least 1,000 mL of blood loss at delivery and received some blood products and/or uterotonic drugs. The use of uterotonic drugs typically includes ergometrine, misoprostol, misoprostol plus oxytocin, carbetocin, ergometrine plus oxytocin and oxytocin on its own. The types of interventions included: 1) trials where they carried out non-pharmacological treatment after failure of administered uterotonic agents (any dosage, route, or regimen) at birth for preventing PPH; and 2) trials evaluating non-pharmacological treatments like uterine packing, balloon tamponade or balloon occlusion, brace suture, vessel ligation, uterine artery ligation, internal iliac artery ligation, Blakemore tube, Bakri® balloon tamponade, or B-lynch or square suture. All non-pharmacologic treatments were divided into 3 groups: Bakri® balloon tamponade, uterine artery embolization and surgical procedures, such as B-lynch, uterine strapping, and compression suture. The compression suture was defined as any method of compression suture, except B-lynch, which is recommended as standard.

3. Outcomes

The main outcome was hysterectomy after birth due to uncontrolled bleeding, calculated as the failure rate of the interventions.

4. Selection and analysis of studies

After the literature search, the reviewers (KJ Lee, K Hong, H Hwang, S Sohn) independently screened the retrieved titles and abstracts. The full text of manuscripts selected for inclusion were examined and the inclusion and exclusion criteria were applied (Fig. 1). Disagreements between reviewers were resolved by consensus or through the participation of a third reviewer.

Reviewers independently extracted the following information from the included studies: author, year and country of publication, number of participants, type of intervention, and outcomes studied (Table 1).

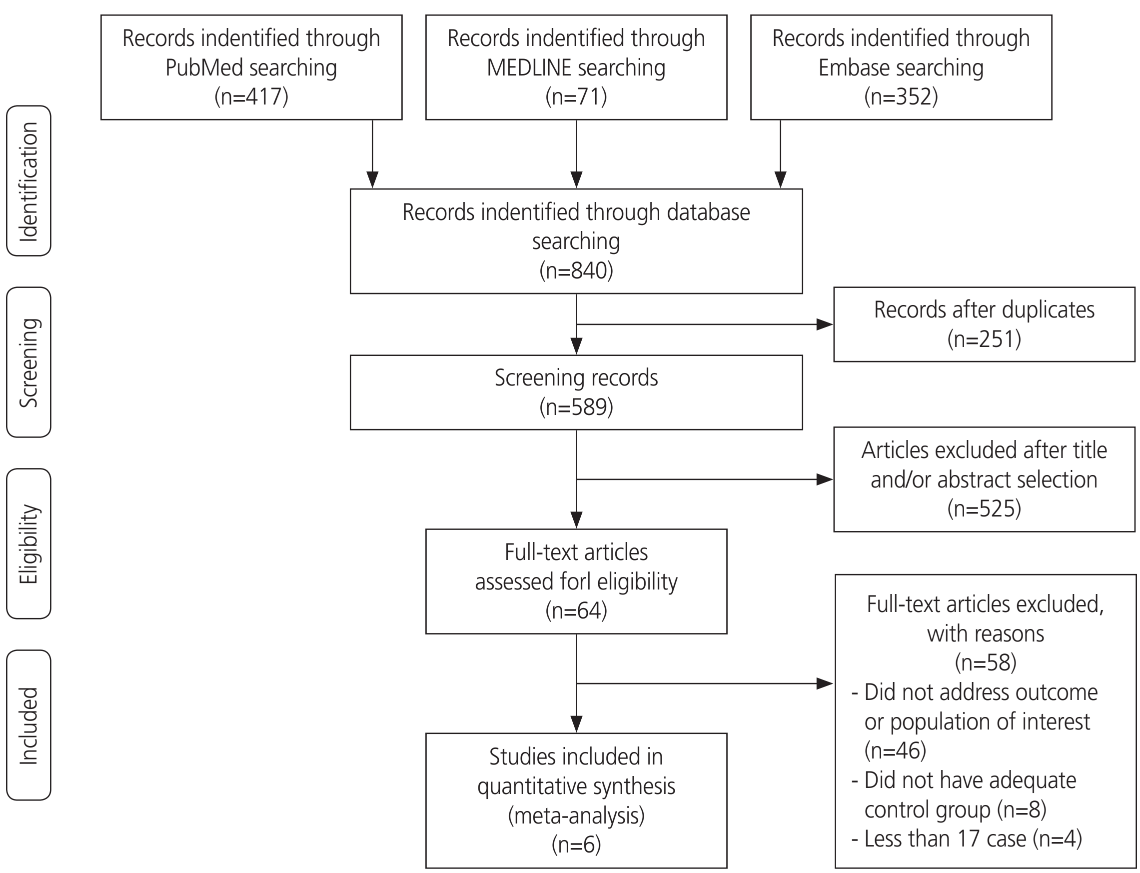

Fig. 1. PRISMA flow chart of study selection process.

Table 1. Characteristics of selected studies

Author	Year of publication	Country	Total number of participants	Type of intervention		Failure rate[a)] (95% CI)	
				Treatment A	Treatment B	Risk A	Risk B
Chai and To [19]	2014	Hong Kong	80	Bakri balloon tamponade	General compression suture	0.26 (0.11–0.46)	0.36 (0.20–0.55)
Feng et al. [20]	2016	China	75	Uterine artery embolization	Uterine strapping General compression suture	0.12 (0.01–0.36)	0.14 (0.06–0.25)
Guo et al. [21]	2018	China	205	Bakri + vaginal gauze	Bakri balloon tamponade	0.04 (0.01–0.08)	0.08 (0.04–0.13)
Howard and Grobman [22]	2015	US	420	Bakri balloon tamponade	Uterine artery embolization	0.10 (0.03–0.23)	0.15 (0.03–0.38)
Yan et al. [26]	2014	China	74	Bakri balloon tamponade	B-lynch	0.05 (0.00–0.26)	0.19 (0.06–0.38)
Zhao et al. [27]	2014	China	87	Bakri balloon tamponade	B-lynch	0.00(0.00–0.06)	0.10 (0.02–0.26)

CI, confidence intervals.
[a)]Failure rate = number of failures/population.

5. Assessing the consistency and quality of included studies

Consistency was tested using the Wald test, which calculated the linearity of regression coefficients for all models [23]. The Revman v5.3 program was used as the Risk of Bias Assessment tool for Non-randomized Studies [24,25]. We assessed 6 parameters including 1) selection of participants, 2) confounding variables, 3) measurement of exposure, 4) blinding of outcome, 5) incomplete outcome data, and 6) selective outcome reporting. Each parameter was graded as unclear, low risk or high risk of bias. Overall bias was considered as "low risk of bias" if the paper was classified as 'low risk' in all domains, "some concerns" if there was at least one domain with a rating of 'some concern', and "high risk of bias" if there was at least one domain with a 'high risk' or several domains with 'some concerns' that could affect the validity of the results. The overall risk of bias was determined according to the previously reported standards [26]. We investigated publication bias using funnel plots, which were visually assessed for symmetry [27]. Finally, an Egger's regression test

Fig. 2. The summary of each study's risk of bias. Green positive icons indicate low risk of bias and red negative icons indicate high risk of bias.

and Begg's test were performed to analyzed the asymmetry of the funnel plot [28].

6. Statistical analysis of network meta-analysis

A network meta-analysis was used to evaluate the effects of various treatments on PPH. Selected publications were reviewed with this method using the frequentist approach. In our study, 2 networks were constructed: network A was based on treatment group type and network B was based on specific treatments. A network diagram was created to demonstrate how each intervention is connected to others through direct comparisons. Within this network diagram, the line width indicates the proportion of patients on a particular treatment, with direct comparison between nodes. Odds ratios (ORs) were summarized as the effect size of each treatment in forest plots. The directions of each treatment were compared with the reference group who had a hysterectomy. Heterogeneity between studies was represented by I^2. We considered I^2 values of more than 50% as indicators of high heterogeneity, but we used random effect models throughout the study since the network meta-analysis of PPH may have had both between and within group variance. However, since the I^2 was 0 in the models used, there were no difference between the random or fixed effect model. The models were used to calculate OR and 95% confidence intervals (CI). For comparison between treatments, each intervention was ranked by the surface under the cumulative ranking curve (SUCRA), known as a *P*-score, which is a frequentist approach to calculate SUCRA without resampling [29]. SUCRA indicates priority where the larger the SUCRA, the better priority. A value of $P<0.05$ was considered statistically significant. Statistical analysis was performed using the 'netmeta' package in R-Studio 1.2.1335 (R studio, Boston, MA, USA).

Results

A total 589 observational studies were initially identified. After screening titles and abstracts, the full text of 64 studies were reviewed, of which 58 were then eliminated. Six studies were finally selected as part of the analyses. Fig. 1 shows the flow of study selection.

The characteristics of the selected publications are summarized in Table 1. The selected publications included 4 studies in China, and one study each in Hong Kong and the USA. Failure to manage bleeding after one or more non-pharmacological treatments leads to postpartum hysterectomy, which was deemed the failure rate. Comparing the B-lynch operation with the use of Bakri balloon tamponade, Yan et al. [30] Chinese study demonstrated the highest failure rate (0.26 vs. 0.185), while the Zhao et al. [31] study observed

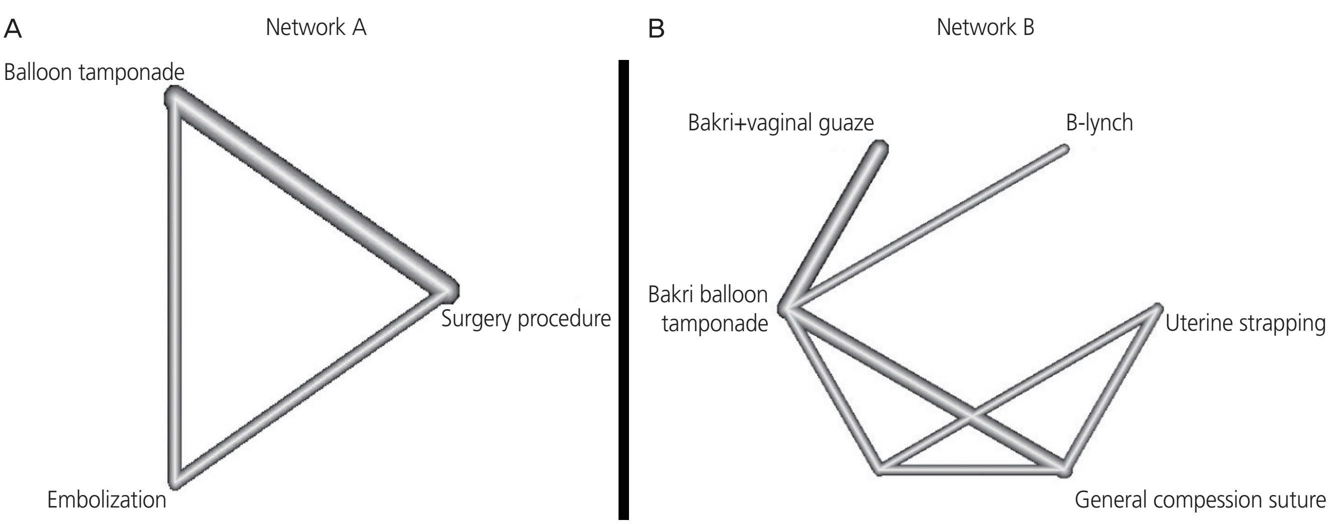

Fig. 3. Network diagrams for postpartum hemorrhage treatments. Nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent an indirect comparison and are line widths are proportional to the number of trials making each indirect comparison. (A) Network A compares 1 type of management, and (B) network B compares complex treatment management.

the lowest failure rate (0 vs. 0.097).

Fig. 2 shows the quality assessment of selected studies. The overall risk of bias was low, except for confounding variables and selective outcome reporting. Feng (2016) and Zhao (2014) did not consider confounding variables. The quality of all studies was reasonable.

Fig. 3 represents direct and indirect relationships among interventions. We also created 2 networks to compare failure rates among studies: the first network grouped by treatment with one management intervention and another network grouped by complex treatments (Fig. 3). The thick line between the balloon tamponade and the surgical procedure represents the most frequent intervention.

Fig. 4 shows indirect and network analysis for PPH treatments. In network A, 3 treatment groups, including balloon tamponade, uterine artery embolization, and surgical procedure, were compared. The surgical procedure was set as the control group, and the balloon tamponade approach was shown to have a 56% lower risk of hysterectomy (OR, 0.44; 95% CI, 0.50–30.54), while uterine artery embolization had 26% lower risk of hysterectomy than the control group (OR, 0.74; 95% CI, 0.22–2.50). In conclusion, non-surgical treatment groups (i.e. Bakri® balloon tamponade, uterine artery embolization) showed a lower failure rate than the surgical group.

In network B, the general compression suture was set as the control group, and compared to all other complex treatments. The B-lynch suture had a risk of hysterectomy that was 4 times higher than general compression suture (OR, 3.91; 95% CI, 0.50–30.54), while uterine artery embolization had 5% lower risk than general compression suture (OR, 0.44; 95% CI, 0.50–30.54). Bakri® balloon tamponade plus vaginal gauze had a failure risk that was 72% lower than general compression suture (OR, 0.28; 95% CI, 0.07–1.18). In conclusion, balloon tamponade and embolization, which were included in the non-surgical treatment group in network A, resulted in a lower failure rate than the control group. On the contrary, B-lynch suture and uterine strapping, which were included in the surgical procedure group in network B, resulted in a higher failure rate than the control group.

The rank of interventions is shown in Table 2. In network A, balloon tamponade ranked higher (0.89 vs. 0.44) than uterine artery embolization. Balloon tamponade had the highest treatment success. In network B, treatments using Bakri (Bakri balloon tamponade plus vaginal gauze and only Bakri balloon tamponade) had the highest ranks (0.95 vs. 0.69 vs.

Table 2. Surface under the cumulative ranking curve (SUCRA): rank of 'network A' treatment groups and 'network B' specific treatments in failure rates

Intervention	SURCA	Rank
Network A		
Balloon tamponade	0.89	1
Uterine artery embolization	0.44	2
Surgery	0.17	3
Network B		
Bakri balloon tamponade + vaginal gauze	0.95	1
Bakri balloon tamponade	0.69	2
Embolization	0.48	3
General compression suture	0.45	4
Uterine strapping	0.34	5
B-lynch	0.09	6

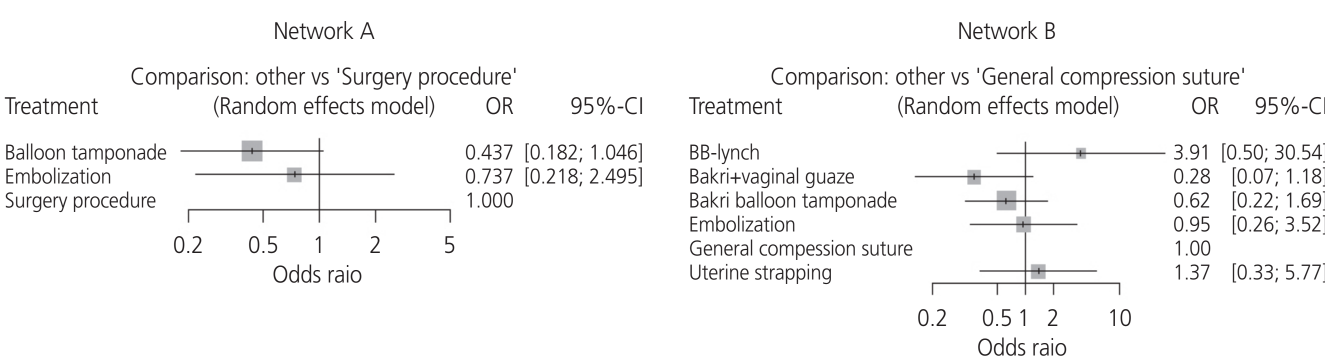

Fig. 4. Forest plot with odd ratios (ORs) and 95% confidence intervals (CIs) from pairwise, indirect and network analysis for postpartum hemorrhage treatments.

0.48) compared with all other treatments.

The consistency test revealed a *P*-value of 0.83 in network A and 0.98 in network B. Thus, our null hypothesis was rejected, indicating that both networks were appropriate. This analysis was repeated for all cases, and no inconsistencies were found. Although the number of included studies was insufficient to determine asymmetry, we found no visual asymmetry in the funnel plots (Fig. 5). Egger's regression test and Begg's test indicated no significant asymmetry, with *P*-value 0.10 and 0.26, respectively.

Discussion

Excessive bleeding after birth is the world's most common cause of death among mothers during childbirth. While most women will have moderate bleeding at birth, others may bleed excessively, which can pose a serious risk to their health and life. To reduce excessive bleeding at birth, the routine use of prophylactic uterotonic drugs has become standard practice worldwide [32].

The use of hysterectomy, the single most dramatically altering procedure, as well as a stressful and surgically challenging procedure, has been a main reason behind low maternal mortality rates in developed countries. The WHO listed peripartum hysterectomy as an identification criterion for "maternal near-miss", which has been introduced as an analytical tool to address health system failures, with the overall goal of improving obstetric care.

In order to guarantee an immediate response and a multidisciplinary team approach, every obstetric practitioner needs to be trained in the management of PPH. Internationally recognized guidelines [33] indicate that one or more second-line measures, including intrauterine (balloon) tamponade, hemostatic brace suturing, ligation of the uterine arteries, and interventional radiology, should be available in hospitals with delivery units and that obstetric practitioners should be familiar with these procedures.

The aim of this study was to provide a new methodology to overcome the limitations of previous systematic reviews and meta-analyses, which only assessed the effect of non-pharmacological treatment, surgical or non-surgical procedures, separately and without considering any prior intervention with pharmacologic treatments. With the network meta-analysis proposed here, these comparisons could be made.

The most recent study on PPH was a systematic review on pharmacological uterotonic agents in prevention of PPH [27]. To our knowledge, this is the first study to conduct a network meta-analysis comparing surgical and non-surgical approaches in the treatment of non-pharmacologic PPH. Considering the effect size of PPH management in each intervention, performing non-surgical treatment prior to surgical treatment helps PPH management. This study is expected to provide further evidence of the effect of non-pharmacological treat-

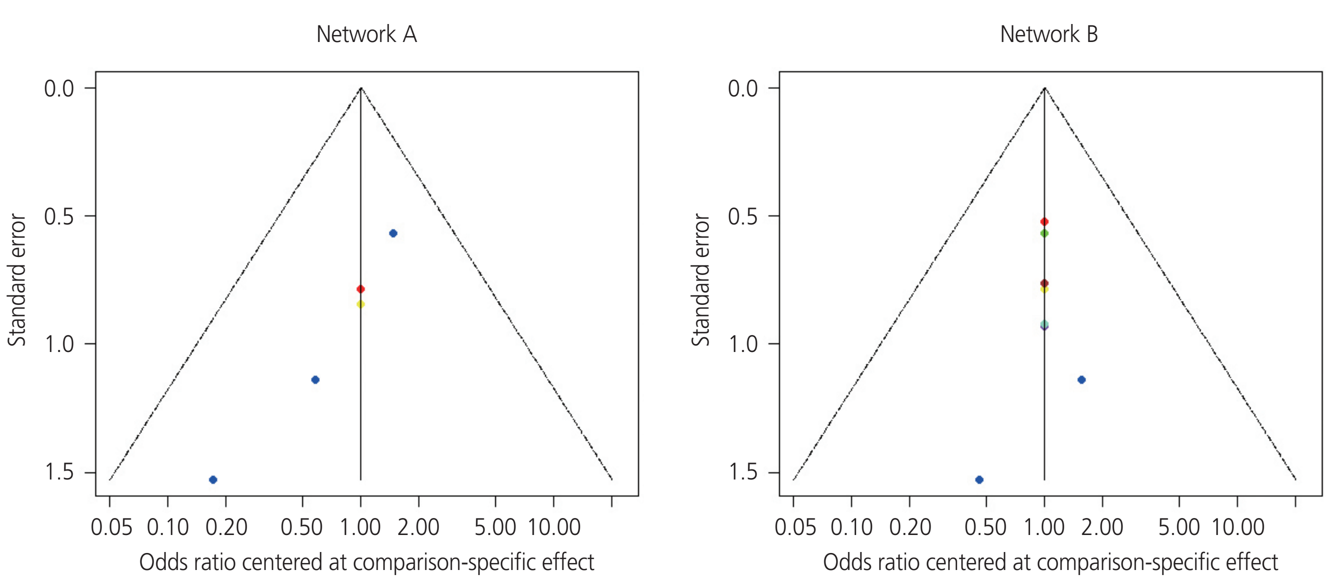

Fig. 5. Funnel plots of selected studies based on treatment grouping.

ment on uncontrolled PPH, and thus help decision making processes carried out by emergent medical professionals and patients. The California Maternal Quality Care Collaborative is actually managed by the OB Hemorrhage Toolkit V20 [33].

Our results are consistent with those of previous studies [34.35]. In PPH, about 80% of patients did not undergo hysterectomy when treated by the Barkley balloon method [34], which suggests that the Barkley balloon method is an appropriate first choice treatment of PPH. On the other hand, uterine artery embolization has treated more than 90% of postpartum bleeding cases, deeming it suitable for the first treatment of postpartum bleeding [35].

This network meta-analysis demonstrates selection bias towards observational studies, due to the difficulty in conducting randomized controlled studies of postpartum bleeding, a life-threatening condition. Consequently, the homogeneity of baseline characteristics of the interventions was not ensured and statistical significance was not achieved, due to the small number of studies. For the same reason, the mode of delivery (i.e. vaginal, cesarean) was not able to be considered as a subgroup. Finally, since there are various reasons for PPH [36] and the effect of treatments may differ, more well-designed studies should be provided to perform a meta-analysis classified by reasons behind why bleeding has occurred.

In conclusion, balloon tamponade is the best method for uncontrolled postpartum bleeding with pharmacologic treatment, followed by embolization and surgical procedures, for the quick treatment of postpartum bleeding.

Acknowledgments

The authors are thankful to the Department of Public Health, Korea University, for their support during the study. And the authors also thank Editage Inc. for their professional language editing service.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Ethical approval

No institutional approval was required because this was an analysis of publicly available data that were produced by Statistics Korea according to the Bioethics and Safety Act (IRB-2019-0014).

Patient consent

Informed consent was not required because this was an analysis of publicly available data that were produced by Statistics Korea according to the Bioethics and Safety Act (IRB-2019-0014).

References

1. Alkema L, Chou D, Hogan D, Zhang S, Moller AB, Gemmill A, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. Lancet 2016;387:462-74.
2. von Herrath MG, Oldstone MB. Virus-induced autoimmune disease. Curr Opin Immunol 1996;8:878-85.
3. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health 2014;2:e323-33.
4. Romero-Gutiérrez G, Espitia-Vera A, Ponce-Ponce de León AL, Huerta-Vargas LF. Risk factors of maternal death in Mexico. Birth 2007;34:21-5.
5. Maraschini A, Lega I, D'Aloja P, Buoncristiano M, Dell'Oro S, Donati S, et al. Women undergoing peripartum hysterectomy due to obstetric hemorrhage: a prospective population-based study. Acta Obstet Gynecol Scand 2020;99:274-82.
6. Rouse DJ, MacPherson C, Landon M, Varner MW, Leveno KJ, Moawad AH, et al. Blood transfusion and cesarean delivery. Obstet Gynecol 2006;108:891-7.
7. World Health Organization. Guideline: delayed umbilical cord clamping for improved maternal and infant health and nutrition outcomes. Geneva: World Health Organization; 2014.
8. Begley CM, Gyte GM, Devane D, McGuire W, Weeks

A, Biesty LM. Active versus expectant management for women in the third stage of labour. Cochrane Database Syst Rev 2019;2:CD007412.
9. Frolova AI, Stout MJ, Tuuli MG, López JD, Macones GA, Cahill AG. Duration of the third stage of labor and risk of postpartum hemorrhage. Obstet Gynecol 2016;127:951-6.
10. Say L, Souza JP, Pattinson RC; WHO working group on Maternal Mortality and Morbidity classifications. Maternal near miss--towards a standard tool for monitoring quality of maternal health care. Best Pract Res Clin Obstet Gynaecol 2009;23:287-96.
11. Byun JM, Kim YN, Jeong DH, Seo YJ, Jeong EJ, Kang JY, et al. Prognosis and indication of emergency hysterectomy following postpartum hemorrhage. Korean J Obstet Gynecol 2012;55:901-6.
12. Mercier FJ, Van de Velde M. Major obstetric hemorrhage. Anesthesiol Clin 2008;26:53-66.
13. Drucker M, Wallach RC. Uterine packing: a reappraisal. Mt Sinai J Med 1979;46:191-4.
14. Bakri YN, Amri A, Abdul Jabbar F. Tamponade-balloon for obstetrical bleeding. Int J Gynaecol Obstet 2001;74:139-42.
15. Tamizian O, Arulkumaran S. The surgical management of postpartum haemorrhage. Curr Opin Obstet Gynecol 2001;13:127-31.
16. B-Lynch C, Coker A, Lawal AH, Abu J, Cowen MJ. The B-Lynch surgical technique for the control of massive postpartum haemorrhage: an alternative to hysterectomy? Five cases reported. BJOG 1997;104:372-5.
17. Yucel O, Ozdemir I, Yucel N, Somunkiran A. Emergency peripartum hysterectomy: a 9-year review. Arch Gynecol Obstet 2006;274:84-7.
18. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med 2015;162:777-84.
19. Chai VY, To WW. Uterine compression sutures for management of severe postpartum haemorrhage: five-year audit. Hong Kong Med J 2014;20:113-20.
20. Feng B, Zhai J, Cai Y. Results of surgical intervention in treating post-cesarean intractable postpartum hemorrhage. Int J Clin Exp Med 2016;9:5154-60.
21. Guo Y, Hua R, Bian S, Xie X, Ma J, Cai Y, et al. Intrauterine Bakri balloon and vaginal tamponade combined with abdominal compression for the management of postpartum hemorrhage. J Obstet Gynaecol Can 2018;40:561-5.
22. Howard TF, Grobman WA. The relationship between timing of postpartum hemorrhage interventions and adverse outcomes. Am J Obstet Gynecol 2015;213:239.e1-3.
23. Shim SR, Kim SJ, Lee J, Rücker G. Network meta-analysis: application and practice using R software. Epidemiol Health 2019;41:e2019013.
24. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.
25. Bilandzic A, Fitzpatrick T, Rosella L, Henry D. Risk of bias in systematic reviews of non-randomized studies of adverse cardiovascular effects of thiazolidinediones and cyclooxygenase-2 inhibitors: application of a new Cochrane risk of bias tool. PLoS Med 2016;13:e1001987.
26. Zhang YJ, Wang N, Gu ZC, Wei AH, Cheng AN, Fang SS, et al. A network meta-analysis for safety of endothelin receptor antagonists in pulmonary arterial hypertension. Cardiovasc Diagn Ther 2019;9:239-49.
27. Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database Syst Rev 2018;12:CD011689.
28. Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 2011;343:d4002.
29. Rücker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. BMC Med Res Methodol 2015;15:58.
30. Yan JY, Zhou ZM, Xu X, Huang XY, Xu RL, Lin SH. Risk factors and surgical interventions associated with primary postpartum haemorrhage unresponsive to first-line therapies. J Obstet Gynaecol 2014;34:588-92.
31. Zhao Y, Zhang Y, Li Z. Appropriate second-line therapies for management of severe postpartum hemorrhage. Int J Gynaecol Obstet 2014;127:180-2.
32. Dahlke JD, Mendez-Figueroa H, Maggio L, Hauspurg AK, Sperling JD, Chauhan SP, et al. Prevention and management of postpartum hemorrhage: a comparison of 4

national guidelines. Am J Obstet Gynecol 2015;213:76.e1-10.
33. California Maternal Quality Care Collaborative. OB hemorrhage toolkit V20. [Internet]. Stanford (CA): California Maternal Quality Care Collaborative; c2015 [cited 2020 March 30]. Available from: https://www.cmqcc.org/resources-tool-kits/toolkits/ob-hemorrhage-toolkit.
34. Kaya B, Tuten A, Daglar K, Misirlioglu M, Polat M, Yildirim Y, et al. Balloon tamponade for the management of postpartum uterine hemorrhage. J Perinat Med 2014;42:745-53.
35. Chen C, Lee SM, Kim JW, Shin JH. Recent update of embolization of postpartum hemorrhage. Korean J Radiol 2018;19:585-96.
36. Oyelese Y, Ananth CV. Postpartum hemorrhage: epidemiology, risk factors, and causes. Clin Obstet Gynecol 2010;53:147-56.