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Original Article

Comparative effectiveness of nonsurgical treatment for stress urinary incontinence in adult women: a systematic review and network meta-analysis of randomized controlled trials

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Abstract: Objective: This study aimed to explore the most effective nonsurgical therapy to treat stress urinary incontinence (SUI). Methods: Data were pooled and the Bayesian random effects model was utilized to evaluate the inconsistencies between indirect and direct proof. Network sub-analyses, sensitivity and subgroup analysis, and standard pairwise comparisons were utilized in preparation of the main analysis. Results: A total of 17 RCTs (852 participants) were enrolled. With regard to therapy, pelvic floor muscle training (PFMT) was more often recommended than biofeedback (BF). The combination of PFMT and BF was remarkably promoted than PFMT alone or PFMT with vaginal cone (VC) or electrical stimulation (ES). The QL scores of patients who underwent PFMT were noticeably improved compared with those of patients who underwent ES. The combination of BF and PFMT was remarkably promoted compared with BF alone. VC was superior to ES with regard to QL scores. By contrast, ES alone was the least preferred method to decrease urine leakage and to promote QL. Conclusion: The combination of BF and PFMT was proven to be an optimal method to treat SUI which aims to promote urine leakage and LQ compared with either PFMT alone, ES, VC, or circular muscle (CME), while ES was the least preferred method to promote LQ.

Keywords: Stress urinary incontinence, network meta-analysis, nonsurgical treatment, pelvic floor muscle training, physical therapies, electrical stimulation, magnetic stimulation, acupuncture

Introduction

According to International Continence Society (ICS), urinary incontinence (UI) is defined as involuntary urine leakage (IUL), which mainly consists of urge incontinence combined with stress incontinence [1] or either urge incontinence alone. Urgency UI (UUI) refers to IUL related to urgency as defined by the International Urogynecological Association and ICS. Furthermore, stress UI (SUI) refers to IUL during physical exertion, application of force, coughing, or sneezing without elevation of detrusor pressure [2] .

Previous studies showed that the prevalence rate of SUI is 40%, which was higher than that of UUI (3%) or mixed UI (MUI) (6.3%) in China [3] . Moreover, SUI can noticeably decrease life quality (LQ). The risk factors of SUI are vaginal delivery, older age, obesity, pregnancy, reinforcing parity, post-menopausal state, and gynecological approaches including hysterectomy [4, 5] . The main nonsurgical methods adopted, which aims to eliminate urine leakage (UL), consist of pelvic floor muscle training (PFMT), vaginal cones (VC), magnetic stimulation (MS), biofeedback (BF), electrical stimulation (ES), and acupuncture alone or in combination with any of the abovementioned methods. The conventional first-line therapy proposed by ICS includes evaluation of pelvic floor strength and application of functional PFMT [6] .

Consequently, this study aimed to compare the effectiveness of those nonsurgical methods when used alone or in combination with another method in reducing UL and promoting LQ in women with SUI.

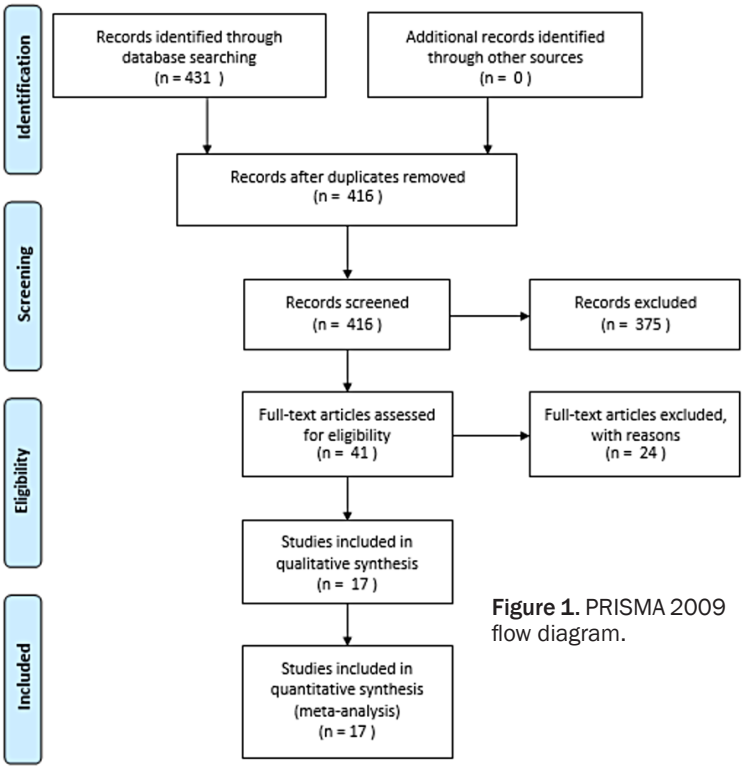

Figure 1. PRISMA 2009 flow diagram.

Materials and methods

Search strategy and article review

MEDLINE and Cochrane databases were screened to search for randomized controlled trials (RCTs) with no limitations to publication time or language according to the algorithm below (see **Appendix**). The most recent searches were carried out in August 2017.

Two researchers (JXL and LZ) independently carried out a primary screening by browsing titles and abstracts and documenting promising entries. Subsequently, the abovementioned researchers independently acquired and evaluated the full texts of every study to search for candidate outcomes aiming at assessment of real eligibility. A discussion was carried out when there was disagreement, which was managed via consensus. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was applied in this study.

Inclusion and exclusion criteria

By searching keywords in the database, RCTs consisting of no less than 2 arms of various therapies of patients with SUI served as candidate studies, while studies exploring effect estimates (EEs) via comparison of nonsurgical methods in women with SUI according to the UI questionnaire (ICI-Q-SF) were included in the meta-analysis. Duplicates were removed and only the most recent studies with the largest sample size (studies adopting overlapping participants) were included.

Titles and abstracts were screened in search of information related to the therapeutic influence of nonsurgical approaches of SUI before acquiring full texts. Cases, case series, letters, narratives, and systematic reviews were eliminated. Studies that failed to distinguish UUI from SUI were also eliminated when obtaining data.

Data isolation and quality evaluation

Two researchers (JXL and LZ) independently acquired study features and data from included studies. The following data were obtained: country, institution, time of data acquisition, inclusion and exclusion criteria, patient features, and therapies.

The quality of evidence for each comparison was evaluated using a risk of bias graph. In short, the instrument to evaluate the risk of bias emphasized seven particular aspects: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias, each of which was categorized as low risk, high risk, or unclear. Review Manager 5.3 software was utilized in order to display the risk of bias graphs [7] .

Statistical analysis

Heterogeneity was determined according to I^2 statistic [8] . With regard to the overall outcome, heterogeneity was evaluated for every pairwise comparison (which consisted of no less than 2 studies) via examination of I^2 statis-

Table 1. The characteristics of the research

Study	Country	Treatments compared	Treatment duration	Patients analyzed per group	Diagnosis of incontinence
Aksac et al. 2003	Turkey	PFMT vs. PFMT + BF	8 wk.	20/20	UD
Aukee et al. 2004	Finland	PFMT vs. PFMT + BF	12 wk.	15/15	UD
Berghmans et al. 1996	Holland	PFMT vs. PFMT + BF	4 wk.	20/20	Clinical and/or UD
Hirakawa et al. 2013	Japan	PFMT vs. PFMT + BF	12 wk.	23/23	Clinical
Morkved et al. 2002	Norway	PFMT vs. PFMT + BF	24 wk.	48/46	UD and pad test
Bo et al. 1999	Norway	PFMT vs. ES	24 wk.	25/25	UD and pad test
Castro et al. 2008	Brazil	PFMT vs. ES vs. VC	24 wk.	26/27/24	UD
Harvey et al. 2006	Canada	PFMT vs. VC	6 wk.	7/7	UD
Pereira et al. 2013	Brazil	PFMT vs. VC	6 wk.	13/15	Clinical
Santos et al. 2009	Brazil	ES vs. VC	16 wk.	24/21	Clinical
Adriane et al. 2017	Brazil	PFMT vs. PFMT + BF	4 wk.	15/16	Clinical
Aysun et al. 2017	Turkey	PFMT vs. PFMT + BF	8 wk.	17/17	Clinical
Laycock et al. 2001	UK	VC vs. BF	12 wk.	41/20	Clinical
Fátima et al. 2016	Brazil	PFMT vs. PFMT + BF	12 wk.	37/35	UD
Oriol et al. 2014	Spain	VC vs. PFMT	24 wk.	35/30	Clinical and/or UD
Robert et al. 2013	The Republic of Poland	ES vs. VC	8 wk.	64/29	Clinical
Wischnitzer et al. 2009	Israel	CME vs. PFMT	12 wk.	28/32	UD

tic. Pooled results were evaluated using the fixed effect model when heterogeneity was insignificant (I^2<50%, P>0.10). By contrast, the random effects model was applied with significant heterogeneity [9] and by default to check for various comparisons that display some degree of heterogeneity.

Our study attempted to evaluate reporting bias and small-study effects using funnel plots of standard errors vs. EEs in terms of primary outcome. Relative EEs from NMA are presented as median differences with a credible interval (CrI) of 95%, which could be regarded as the conventional mean difference (MD) and confidence interval (CI), respectively. The results of the 1-hour pad-test conducted in every SUI patient in each study was obtained and pooled using the Bayesian fixed effects model with a minimally informative prior distribution of related therapeutic influence. Node-splitting approach was utilized to evaluate the consistency of indirect and direct sources of proof in the network [10] . If the CrIs do not cross the effect line, the consistency has statistical significance.

EEs of NMA were displayed as forest plots in terms of not only binary but also continuous outcome. Surface under the cumulative ranking (SUCRA) values were evaluated to determine if a certain therapeutic method is optimal than other methods. However, it did not actually mean that it was appropriate to apply this method to patients with other crucial clinical features, which were not included in the analysis. It was more potential to be the optimal choice with SUCRA closer to 100 while it was more potential to be poorer with SUCRA closer to 0 [11] .

Results

Study search and study features

The flow diagram is shown in **Figure 1** (PRISMA 2009 Flow Diagram) in conformity to PRISMA-NMA statement. About 431 studies were obtained subsequent to database screening. A total of fifteen duplicates were eradicated while 335 studies were eliminated due to titles and abstracts failing to meet the preliminarily proposed selection criteria during primary examination. The full texts of 41 studies were evaluated, of which 24 were eliminated: 3 overlapping participants, 5 reviews, and sixteen studies that failed to distinguish SUI from UUI. In the end, a total of 17 RCTs were included in our network meta-analysis [12-28] .

Essential features of included research are displayed in **Table 1**, which consisted of study design, therapeutic approaches, incontinence

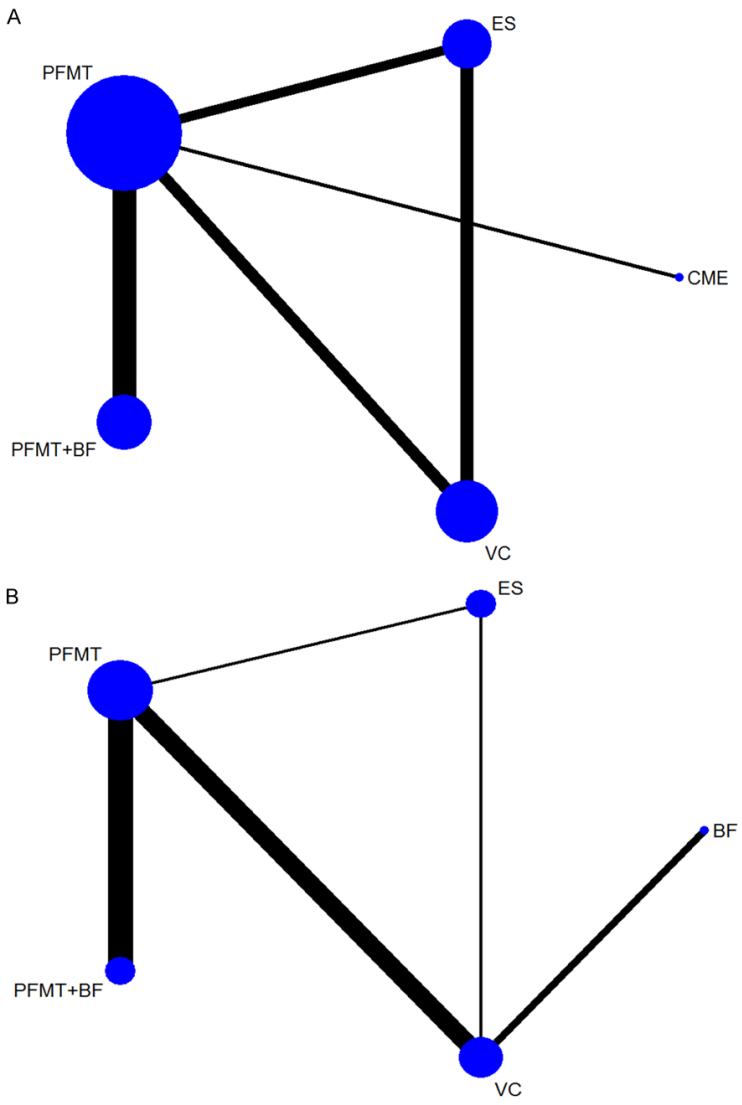

Figure 2. A. A network of nonsurgical methods compared based on the results of pad-test in the network meta-analysis; B. A network of nonsurgical methods compared based on LQ scores in the network meta-analysis.

diagnosis, sample size, and therapy period. The included studies were published from 1996 to 2017. Three studies only enrolled women in the post-menopausal period. All studies included patients of various races, such as white, Asian, and mixed race. One study conducted three comparison interventions, while the others included two. Patients with SUI underwent random classification and received various therapeutic approaches such as PFMT, ES, CME, BF, and VC.

Results of pad tests and LQ scores are shown (**Figure 2A** and **2B**).

Risk of bias

All studies were at low risk of bias due to random sequence generation, while 11 studies (65%) were at low risk of bias due to allocation concealment. Only two studies (12%) were at low risk of bias not only due to blinding of participants but also due to outcome evaluation. The results of the evaluation of risk of bias are presented in **Figure 3A** and **3B**.

Network meta-analysis

This study consisted of 17 RCTs including 852 women, of which all explored pad tests while 11 investigated the LQ scores.

Network analysis: 1-hour pad test

No less than two kinds of nonsurgical methods were compared directly in the included studies. A total of 8 events took place in 450 patients who were randomly assigned to PFMT (154), BF (75), combination of PFMT and BF (75), VC (97), CME (28). The outcome of analysis is displayed in **Figures 4**, **5A** and **5B**. PFMT was noticeably increased subsequent to therapy compared with BF. A combination of both was superior to either PFMT alone and ES or VC based on the results of the 1-hour pad test. Combination of PFMT and BF could serve as the optimal nonsurgical approach in treating women with SUI and in reducing UL.

Network analysis of LQ

The outcome of network analysis of QL is shown in **Figures 6** and **7A**, **7B**. A total of 402 patients, who were randomly assigned to PFMT (122), BF (49), combination of both PFMT and BF (91), VC (76), and ES (64), experienced 7 adverse events. PFMT was noticeably promoted as a

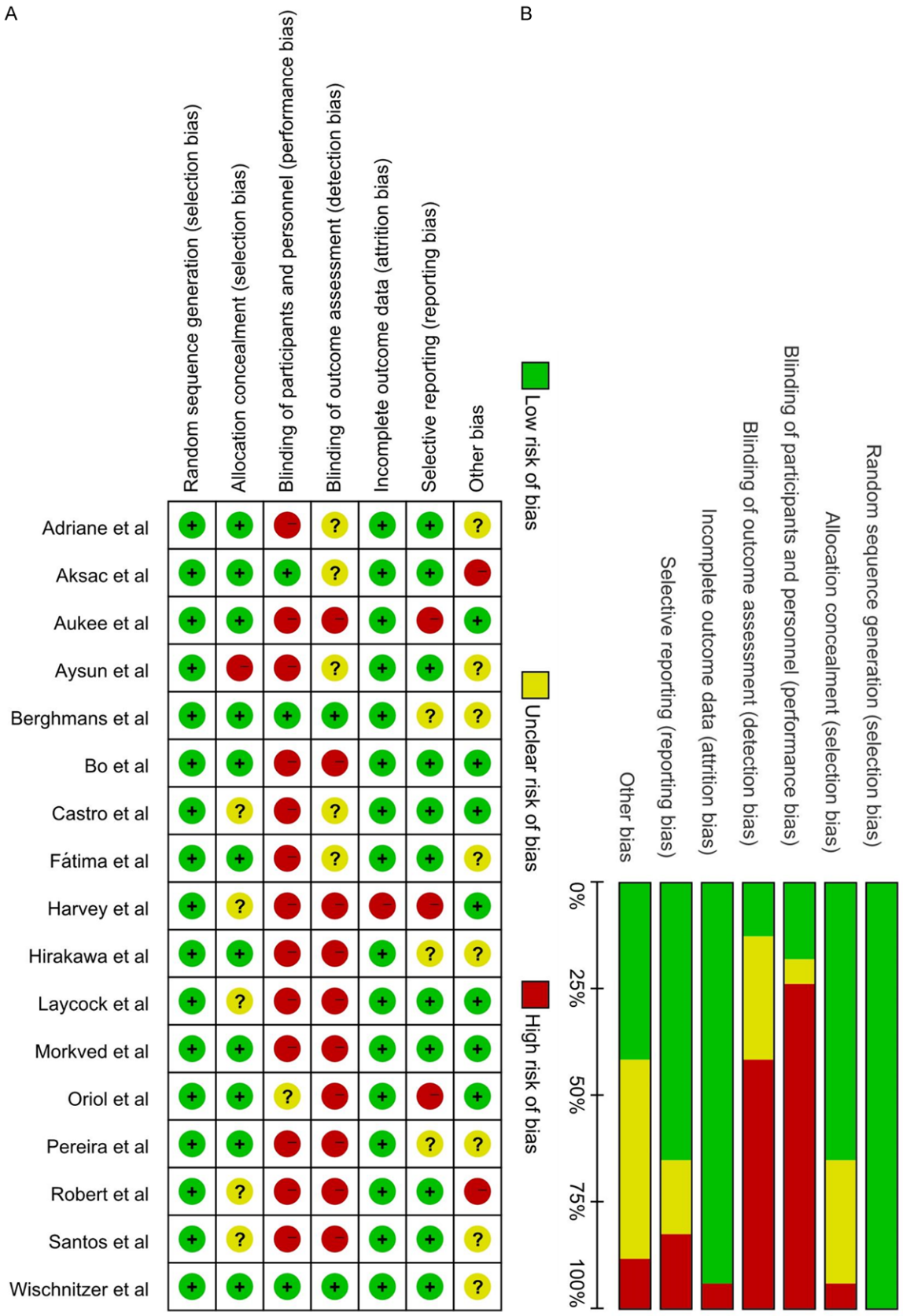

Figure 3. A. Risk of bias evaluation; B. Risk of bias evaluation.

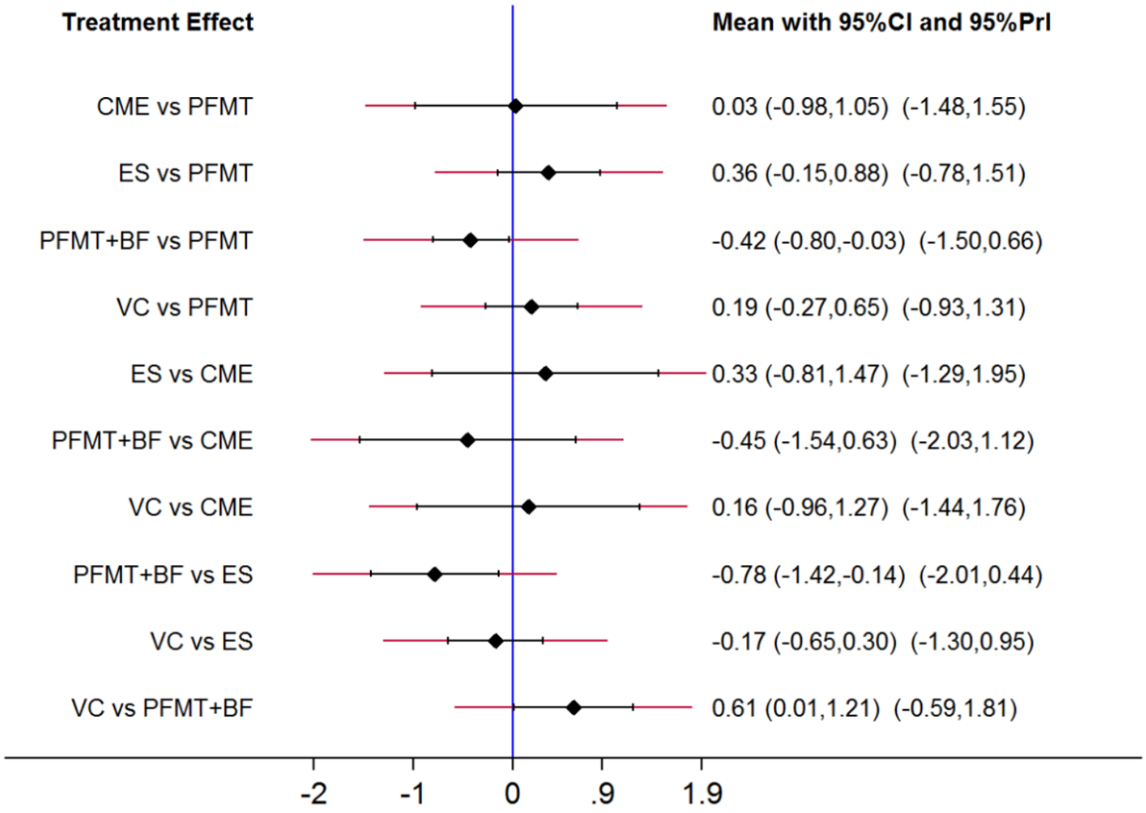

Figure 4. Forest plot for comparison of nonsurgical methods via 1-hour pad test.

subsequent therapy over ES. A combination of PFMT and BF was superior to either PFMT or BF alone, while VC was remarkably superior to ES in terms of QL scores. Combination of PFMT and BF could serve as the optimal nonsurgical approach to treat women suffering from SUI and to promote QL, while ES was the least preferred method (**Figure 8**).

Quantity

One-hour pad test group: A: CME; B: ES; C: PFMT; D: PFMT + BF; E: VC.

The influence of direct comparison results of different control measures on the results of mesh meta-analysis of different control measures (**Figure 8A**).

Consistency test analysis showed that as to the literature included in one-hour pad test group, there is good consistency between the directly compared evidence and the indirect compared evidence (**Figure 9A**).

The funnel plot shows that the literature included in the urine pad test group did not have significant publication bias (**Figure 10A**).

LQ group: A: BF; B: ES; C: PFMT; D: PFMT + BF; E: VC.

The influence of direct comparison results of different control measures on the results of mesh meta-analysis of different control measures (**Figure 8A**).

Consistency test analysis showed that as to the literature included in LQ group, there is good consistency between the directly compared evidence and the indirect compared evidence (**Figure 9A**).

The funnel plot shows that the literature included in the LQ group did not have significant publication bias (**Figure 10A**).

Discussion

This study reported all available evidence that proved the therapeutic efficacy of the following approaches in treating women with SUI: PFMT, ES, CME, BF, and VC. This network meta-analy-

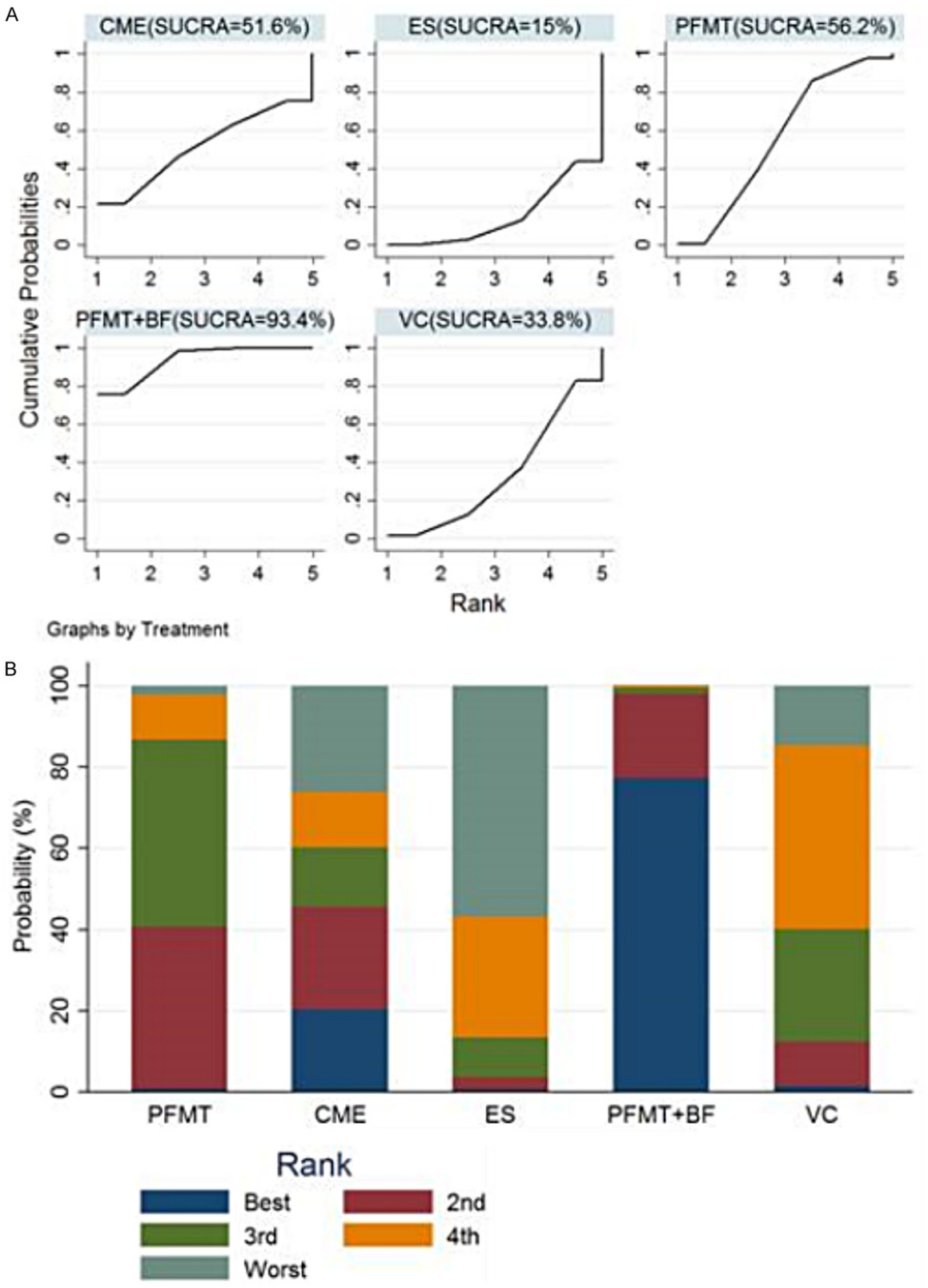

Figure 5. A. Surface under the cumulative ranking outcome for comparison of nonsurgical methods via 1-hour pad test. B. Bar diagram for ranking the outcome for comparison of nonsurgical methods via 1-hour pad test.

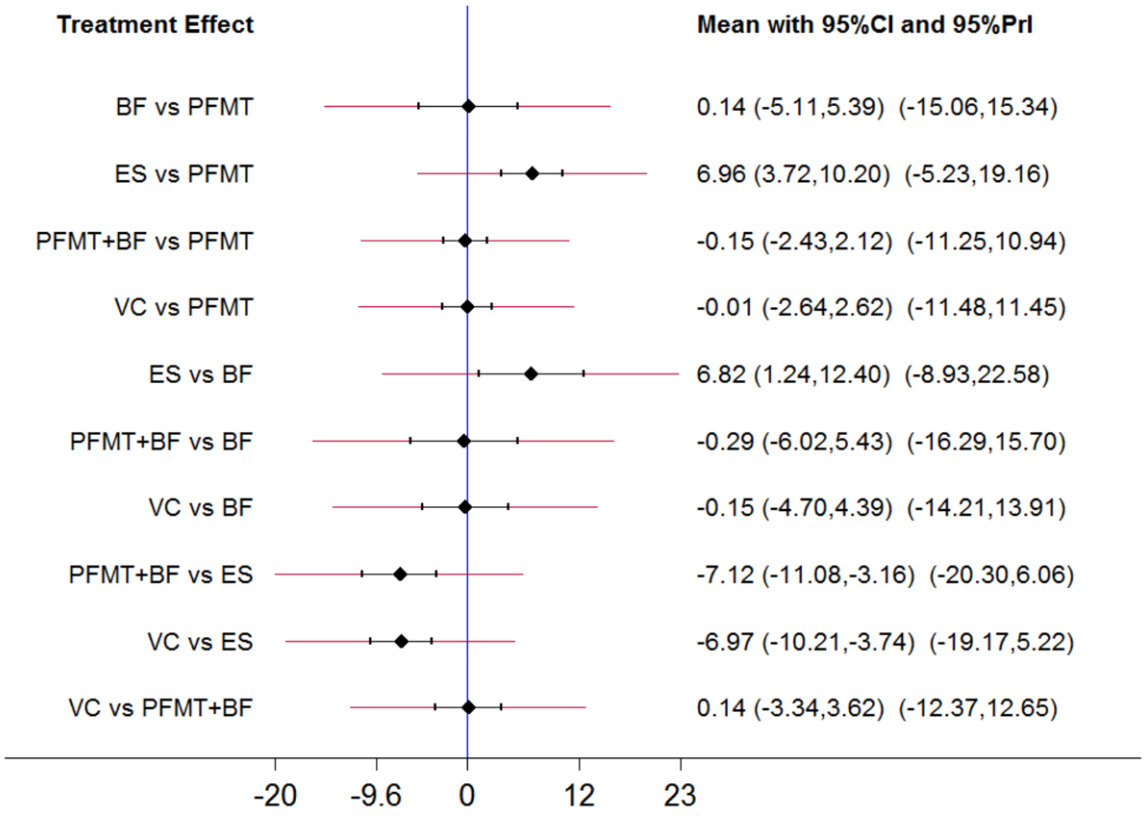

Figure 6. Forest plot for comparison of nonsurgical methods via LQ score.

sis included seventeen studies enrolling 880 patients. It was indicated in our research that a combination of PFMT and BF noticeably decreased UL and improved LQ in comparison to other therapeutic methods for treatment of SUI. Studies that explored SUI for a period of 4-24 weeks were included in our research since 12 weeks served as the most prevalent time to examine the influence of SUI therapy. The diagnosis of SUI was carried out clinically and/or relied on urodynamics and/or pad test. All patients enrolled were women.

The NICE guidelines indicated that trials of PFMT of less than 3 months as first-line therapy in women with SUI or MUI must be provided. Furthermore, the combination of ES and PFMT must be regard as a treatment of choice. ES and/or BF will be taken into consideration when patients are unable to actively contract their pelvic floor muscles to improve motivation and thus adherence to treatment [29] . However, guidelines failed to reveal the influence of other nonsurgical approaches. Such findings comply with other systemic reviews exploring this field [30, 31] , but our study is the first to utilize network meta-analysis that aimed to explore the difference between various types of nonsurgical approaches.

Our study indicates that PFMT is a more appropriate subsequent therapy than BF. The combination of BF and PFMT is superior to BF, PFMT, ES, or VC alone based on the results of the 1-hour pad test. PFMT is remarkably superior to ES in terms of LQ. The combination of BF and PFMT is noticeably superior to BF alone, while VC is superior to ES. Collectively, a combination of PFMT and BF seems the optimal choice in treatment of SUI, decreasing UL, and promoting LQ.

There are some limitations in our meta-analysis, including the different qualities of included studies as well as publication biases. Whether included studies resemble each other enough to allow for appropriate comparison for every target outcome is a crucial consideration for any NMA. Consequently, our study included promising researches that resemble one anoth-

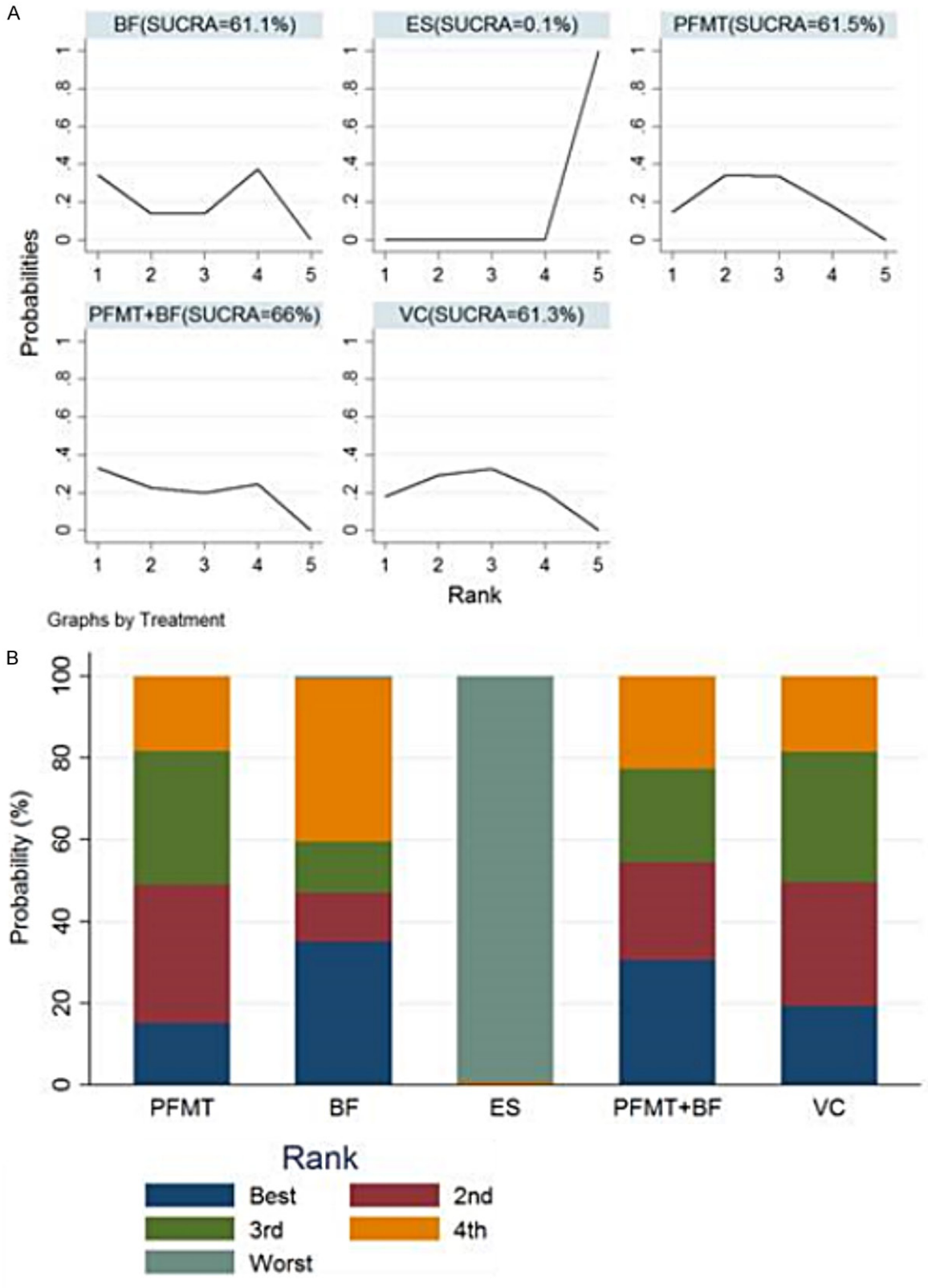

Figure 7. A. Surface under the cumulative ranking outcome for comparison of nonsurgical methods via LQ score; B. Bar diagram for ranking outcome for comparison of nonsurgical methods via LQ score.

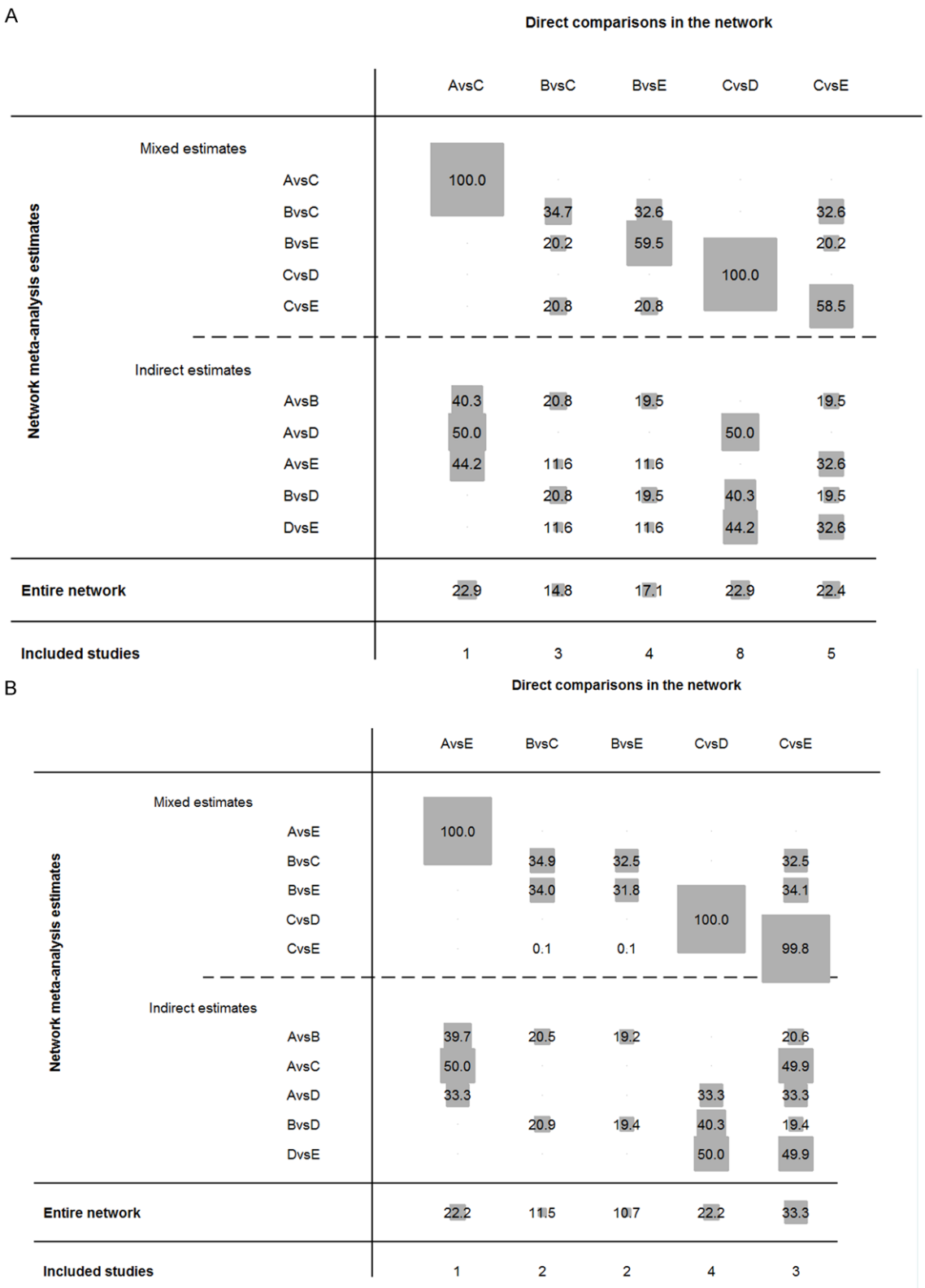

Figure 8. A. Contribution plot for 1-hour pad test group, A: CME; B: ES; C: PFMT; D: PFMT + BF; E: VC; B. Contribution plot for LQ group, A: BF; B: ES; C: PFMT; D: PFMT + BF; E: VC.

er in terms of methodological quality, participants, therapies, and outcome examination. It was revealed via evaluation of risk of bias that all RCTs were at low risk of bias in terms of ran-

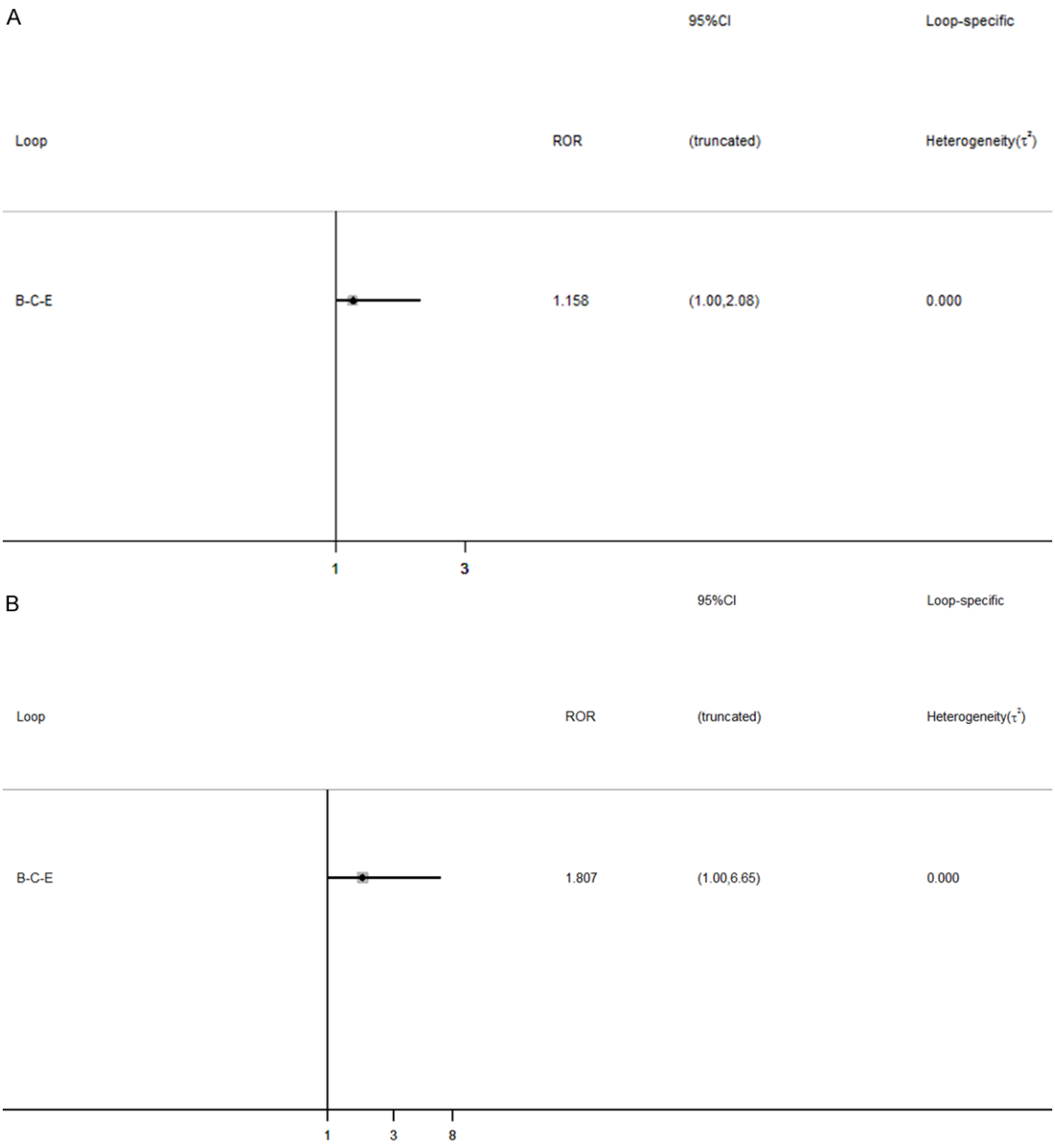

Figure 9. A. Risk of bias graphs for 1-hour pad test group, A: CME; B: ES; C: PFMT; D: PFMT + BF; E: VC; B. Risk of bias graphs for LQ group, A: BF; B: ES; C: PFMT; D: PFMT + BF; E: VC.

dom sequence generation, while 11 (65%) were at low risk of bias with regard to allocation concealment. Only two RCTs (12%) were at low risk of bias in terms of not only blinding of participants but also outcome evaluation.

To begin with, this research enrolled studies that merely assessed the therapeutic effect of 1-hour pad test or LQ, which could have restricted the quantity of possible comparisons. Nevertheless, our study excluded non-randomized trials in fear of concerns that those researches may possibly bring about bias of EEs due to confounders generated from shortage of randomization. In this study, the quality of evidence was downgraded mainly because of indirect network connectivity between therapies, limited sample size, participant blinding, and outcome evaluation. Moreover, no differentiation between home PFMT and overseen PFMT was carried out.

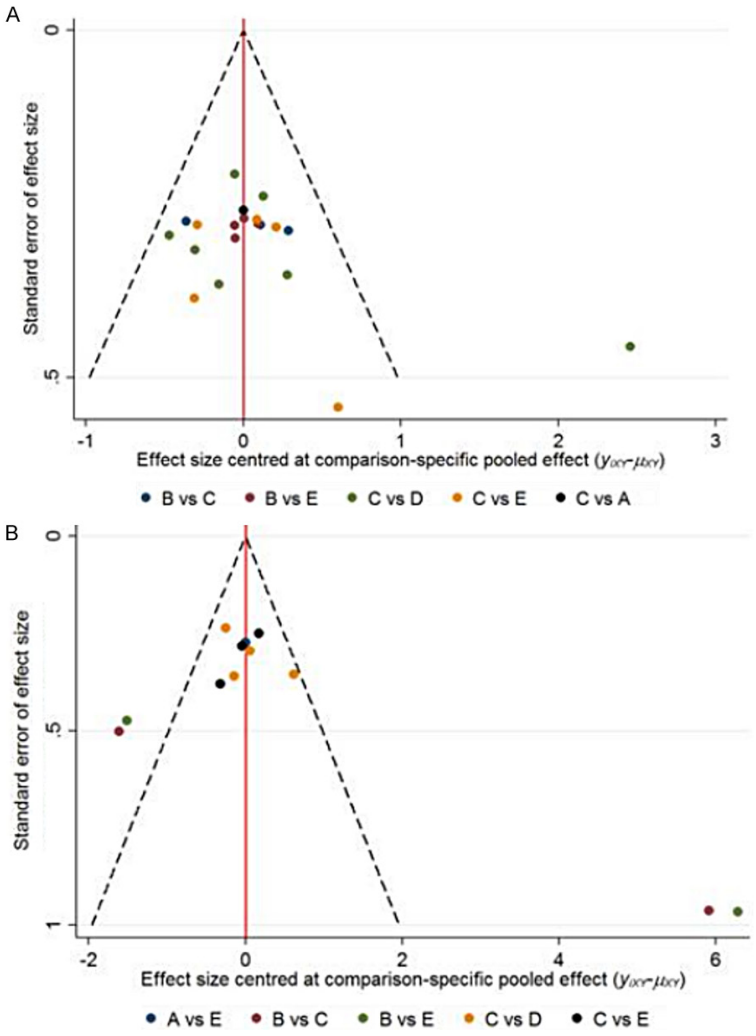

Figure 10. A. Funnel plot for 1-hour pad test group, A: CME; B: ES; C: PFMT; D: PFMT + BF; E: VC; B. Funnel plot for LQ group, A: BF; B: ES; C: PFMT; D: PFMT + BF; E: VC.

Conclusions

The combination of PFMT and BF serves as the optimal approach to treat women with SUI, reduce UL, and promote LQ after comparing various nonsurgical methods, such as PFMT, ES, BF, CME, VS, and PFMT + BF. ES was the least preferred method to promote LQ. Thus, it is necessary to develop more supporting proof from RCTs, which were well designed and performed and which evaluated the efficacy outcome and adverse events during similar periods with the help of similar detection methods.

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Disclosure of conflict of interest

None.

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Appendix: Search Strategy

Databases: MEDLINE and Cochrane databases

Date of search: August 31, 2017

((((((kegel [All Fields] OR ("biofeedback, psychology" [MeSH Terms] OR ("biofeedback" [All Fields] AND "psychology" [All Fields]) OR "psychology biofeedback" [All Fields] OR "biofeedback" [All Fields])) OR ("electric stimulation" [MeSH Terms] OR ("electric" [All Fields] AND "stimulation" [All Fields]) OR "electric stimulation" [All Fields] OR ("electrical" [All Fields] AND "stimulation" [All Fields]) OR "electrical stimulation" [All Fields])) OR (magenetic [All Fields] AND stimulation [All Fields])) OR ("massage" [MeSH Terms] OR "massage" [All Fields])) OR ("Chin Med" [Journal] OR ("chinese" [All Fields] AND "medicine" [All Fields]) OR "chinese medicine" [All Fields])) AND ("urinary incontinence" [MeSH Terms] OR ("urinary" [All Fields] AND "incontinence" [All Fields]) OR "urinary incontinence" [All Fields])) AND ("Randomized Controlled Trial" [Publication Type] OR "Random Allocation" [Mesh] OR "Single-Blind Method" [Mesh] OR "Double- Blind Method" [Mesh] OR "Cross-Over Studies" [Mesh] OR "Placebos" [Mesh] OR (random [TIAB] OR random' [TIAB] OR random1 [TIAB] OR random1y [TIAB] OR randomally [TIAB] OR randomaly [TIAB] OR randomamplified [TIAB] OR randoman [TIAB] OR randomand [TIAB] OR randomate [TIAB] OR randombalance [TIAB] OR randombased [TIAB] OR randomboost [TIAB] OR randombred [TIAB] OR randombreds [TIAB] OR randomcoil [TIAB] OR randomcommittee [TIAB] OR randomdata [TIAB] OR randomdigit [TIAB] OR randomdock [TIAB] OR randomdot [TIAB] OR randome [TIAB] OR randomed [TIAB] OR randomeffects [TIAB] OR randomely [TIAB] OR randomer [TIAB] OR randomesque [TIAB] OR randomezed [TIAB] OR randomforest [TIAB] OR randomforest' [TIAB] OR randomforest4life [TIAB] OR randomforests [TIAB] OR randomforrest [TIAB] OR randomfrog [TIAB] OR randomglm [TIAB] OR randomi [TIAB] OR randomiazed [TIAB] OR randomic [TIAB] OR randomically [TIAB] OR randomicaly [TIAB] OR randomicamente [TIAB] OR randomiced [TIAB] OR randomicity [TIAB] OR randomico [TIAB] OR randomided [TIAB] OR randomied [TIAB] OR randomifzed [TIAB] OR randomil [TIAB] OR randomily [TIAB] OR randomin [TIAB] OR randomined [TIAB] OR randomingly [TIAB] OR randominization [TIAB] OR randominzed [TIAB] OR randomirrespective [TIAB] OR randomis [TIAB] OR randomisable [TIAB] OR randomisaion [TIAB] OR randomisation [TIAB] OR randomisation' [TIAB] OR randomisations [TIAB] OR randomisationsecondary [TIAB] OR randomisd [TIAB] OR randomise [TIAB] OR randomised [TIAB] OR randomised' [TIAB] OR randomisedbhc [TIAB] OR randomisedcontrolled [TIAB] OR randomisedrandomised [TIAB] OR randomisee [TIAB] OR randomisees [TIAB] OR randomisely [TIAB] OR randomises [TIAB] OR randomisiert [TIAB] OR randomisierte [TIAB] OR randomisierten [TIAB] OR randomisierter [TIAB] OR randomisierung [TIAB] OR randomising [TIAB] OR randomisized [TIAB] OR randomisly [TIAB] OR randomiz [TIAB] OR randomizability [TIAB] OR randomizable [TIAB] OR randomizacao [TIAB] OR randomizad [TIAB] OR randomizadas [TIAB] OR randomizadely [TIAB] OR randomizado [TIAB] OR randomizados [TIAB] OR randomizaion [TIAB] OR randomization [TIAB] OR randomization' [TIAB] OR randomization's [TIAB] OR randomizationin [TIAB] OR randomizations [TIAB] OR randomizations' [TIAB] OR randomizationstudies [TIAB] OR randomizd [TIAB] OR randomize [TIAB] OR randomize' [TIAB] OR randomized [TIAB] OR randomized' [TIAB] OR randomized150 [TIAB] OR randomizedcontrolled [TIAB] OR randomizedcontrolledtrials [TIAB] OR randomizedcontroltrials [TIAB] OR randomizedcrossover [TIAB] OR randomizeddouble [TIAB] OR randomizedduring [TIAB] OR randomizedinto [TIAB] OR randomizedly [TIAB] OR randomizedphase [TIAB] OR randomizedsequence [TIAB] OR randomizedto [TIAB] OR randomizedtrial [TIAB] OR randomizely [TIAB] OR randomizer [TIAB] OR randomizer' [TIAB] OR randomizers [TIAB] OR randomizes [TIAB] OR randomizied [TIAB] OR randomizing [TIAB] OR randomizing' [TIAB] OR randomizingly [TIAB] OR randomjungle [TIAB] OR randoml [TIAB] OR randomlike [TIAB] OR randomlly [TIAB] OR randomly [TIAB] OR randomly' [TIAB] OR randomly'assign [TIAB] OR randomlyand [TIAB] OR randomlyassigned [TIAB] OR randomlydivided [TIAB] OR randomlyequally [TIAB] OR randomlyinserted [TIAB] OR randomlyselected [TIAB] OR randomlysplit [TIAB] OR randomlyuniformly [TIAB] OR randommess [TIAB] OR randommethacrylic [TIAB] OR randommized [TIAB] OR randommobility [TIAB] OR randomnes [TIAB] OR randomness [TIAB] OR randomness' [TIAB] OR randomnesses [TIAB] OR randomnicity [TIAB] OR randomniized [TIAB] OR randomnized [TIAB] OR randomnly [TIAB] OR randomomized [TIAB] OR randomosed [TIAB] OR randomoutcross [TIAB] OR randomozed [TIAB] OR randompairs [TIAB] OR randompattern [TIAB] OR randompf [TIAB] OR randomphase [TIAB] OR randompod [TIAB] OR randompolypeptides [TIAB] OR randompower [TIAB] OR randoms

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[TIAB] OR blindsided [TIAB] OR blindsidedness [TIAB] OR blindsides [TIAB] OR blindsiding [TIAB] OR blindsight [TIAB] OR blindsight' [TIAB] OR blindsighted [TIAB] OR blindsighters [TIAB] OR blindsighters' [TIAB] OR blindsmell [TIAB] OR blindsnake [TIAB] OR blindsnakes [TIAB] OR blindspot [TIAB] OR blindspot' [TIAB] OR blindspotesotropia [TIAB] OR blindspots [TIAB] OR blindspots' [TIAB] OR blindstudy [TIAB] OR blindtrack [TIAB] OR blindtrial [TIAB] OR blindversuch [TIAB] OR blindwalking [TIAB] OR blindwell [TIAB] OR blindworm [TIAB] OR blindy [TIAB])) OR ("open" [TIAB] AND (label [TIAB] OR label' [TIAB] OR label" [TIAB] OR label's [TIAB] OR label2 [TIAB] OR labela [TIAB] OR labelability [TIAB] OR labelable [TIAB] OR labelagriwaste [TIAB] OR labeland [TIAB] OR labelat-

laseditor [TIAB] OR labelatol [TIAB] OR labelbased [TIAB] OR labeld [TIAB] OR labele [TIAB] OR labeled [TIAB] OR labeled' [TIAB] OR labeled1 [TIAB] OR labeledb [TIAB] OR labeledd [TIAB] OR labeledhuman [TIAB] OR labeledin [TIAB] OR labeledstaph [TIAB] OR labeledtransfer [TIAB] OR labeledwith [TIAB] OR labeledz9 [TIAB] OR labeleed [TIAB] OR labelel [TIAB] OR labeleled [TIAB] OR labeler [TIAB] OR labeler's [TIAB] OR labelers [TIAB] OR labelers' [TIAB] OR labeles [TIAB] OR labeless [TIAB] OR labeless' [TIAB] OR labelfree [TIAB] OR labelhash [TIAB] OR labeli [TIAB] OR labeliing [TIAB] OR labelin [TIAB] OR labelind [TIAB] OR labeline [TIAB] OR labeling [TIAB] OR labeling' [TIAB] OR labeling's [TIAB] OR labelingc [TIAB] OR labelingchanges [TIAB] OR labelingdeplasticized [TIAB] OR labelingepoxy [TIAB] OR labelingg [TIAB] OR labelinglr [TIAB] OR labelingof [TIAB] OR labelingpositive [TIAB] OR labelingprocedures [TIAB] OR labelings [TIAB] OR labelingsoliduselectron [TIAB] OR labelingstaining [TIAB] OR labelingtime [TIAB] OR labelingvpa [TIAB] OR labelinig [TIAB] OR labelinto [TIAB] OR labelised [TIAB] OR labelising [TIAB] OR labelit [TIAB] OR labelization [TIAB] OR labelized [TIAB] OR labelizes [TIAB] OR labell [TIAB] OR labella [TIAB] OR labellable [TIAB] OR labellae [TIAB] OR labellaed [TIAB] OR labellar [TIAB] OR labelld [TIAB] OR labelle [TIAB] OR labelle' [TIAB] OR labellectomized [TIAB] OR labelled [TIAB] OR labelled' [TIAB] OR labelledalpha [TIAB] OR labelledc6 [TIAB] OR labelledd [TIAB] OR labelledin [TIAB] OR labelledlabeled [TIAB] OR labelledminute [TIAB] OR labelledt [TIAB] OR labeller [TIAB] OR labellers [TIAB] OR labelles [TIAB] OR labelless [TIAB] OR labellicula [TIAB] OR labellig [TIAB] OR labellin [TIAB] OR labelling [TIAB] OR labelling' [TIAB] OR labellingof [TIAB] OR labellings [TIAB] OR labellisation [TIAB] OR labellized [TIAB] OR labellling [TIAB] OR labelllng [TIAB] OR labelloid [TIAB] OR labellulid [TIAB] OR labellum [TIAB] OR labellumto [TIAB] OR labelmap [TIAB] OR labelmaps [TIAB] OR labelme [TIAB] OR labelmg [TIAB] OR labelmonoclonal [TIAB] OR labelpepmatch [TIAB] OR labelphysiologically [TIAB] OR labels [TIAB] OR labels' [TIAB] OR labelstudy [TIAB] OR labeltalol [TIAB] OR labelted [TIAB] OR labelum [TIAB] OR labelwise [TIAB])) OR (factorial [TIAB] OR factorial' [TIAB] OR factoriales [TIAB] OR factoriality [TIAB] OR factorialization [TIAB] OR factorialized [TIAB] OR factorially [TIAB] OR factorials [TIAB]) OR (assign [TIAB] OR assign' [TIAB] OR assign1 [TIAB] OR assignability [TIAB] OR assignable [TIAB] OR assignalbe [TIAB] OR assignate [TIAB] OR assignated [TIAB] OR assignation [TIAB] OR assignations [TIAB] OR assignd [TIAB] OR assigne [TIAB] OR assigned [TIAB] OR assigned' [TIAB] OR assigned11 [TIAB] OR assignee [TIAB] OR assignee's [TIAB] OR assignees [TIAB] OR assignement [TIAB] OR assignements [TIAB] OR assignemnt [TIAB] OR assignemnts [TIAB] OR assigner [TIAB] OR assigners [TIAB] OR assigners' [TIAB] OR assignes [TIAB] OR assignfit [TIAB] OR assignificant [TIAB] OR assignificantly [TIAB] OR assignig [TIAB] OR assigning [TIAB] OR assigninga [TIAB] OR assignis [TIAB] OR assignmenents [TIAB] OR assignment [TIAB] OR assignment' [TIAB] OR assignment's [TIAB] OR assignment1 [TIAB] OR assignmentchecker [TIAB] OR assignmentof [TIAB] OR assignments [TIAB] OR assignments' [TIAB] OR assignmentsof [TIAB] OR assignmentxtopic [TIAB] OR assignmetit [TIAB] OR assigns [TIAB] OR assigns' [TIAB] OR assignsubsets [TIAB] OR assignxlink [TIAB]) OR (allocate [TIAB] OR allocated [TIAB] OR allocated' [TIAB] OR allocatelli [TIAB] OR allocatelliglobosispora [TIAB] OR allocaters [TIAB] OR allocates [TIAB]) OR (volunteer [TIAB] OR volunteer' [TIAB] OR volunteer's [TIAB] OR volunteerd [TIAB] OR volunteered [TIAB] OR volunteered' [TIAB] OR volunteeres [TIAB] OR volunteerget [TIAB] OR volunteering [TIAB] OR volunteering' [TIAB] OR volunteering's [TIAB] OR volunteerism [TIAB] OR volunteerism' [TIAB] OR volunteerisms [TIAB] OR volunteerist [TIAB] OR volunteers [TIAB] OR volunteers' [TIAB] OR volunteers'diagnosis [TIAB] OR volunteers'homes [TIAB] OR volunteers'right [TIAB] OR volunteers's [TIAB] OR volunteers'sera [TIAB] OR volunteersadministered [TIAB] OR volunteersfor [TIAB] OR volunteerswere [TIAB])).