



Review

Comparative efficacy and safety of different circumcisions for patients with redundant prepuce or phimosis: A network meta-analysis



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HIGHLIGHTS

- The effect of three circumcisions (CC, SRC and DCSD) on redundant prepuce or phimosis has not been conclusively studied in previous researches.
- The study had collected high-quality RCTs in order to conduct an overall NMA for comparative safety and efficacy in three treatments.
- The analysis shows a significant increase in the satisfaction of postoperative penile appearance after the therapy of novel circumcisions (SRC, DCSD), comparing with CC.
- The network meta-analysis confirmed that the disposable circumcision suture device could be the best choice for patients with phimosis or redundant prepuce.

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ABSTRACT

Background: Phimosis and redundant prepuce are defined as the inability of the foreskin to be retracted behind the glans penis in uncircumcised males. To synthesize the evidence and provide the hierarchies of different circumcisions for phimosis and redundant prepuce, we performed an overall network meta-analysis (NMA) based on their comparative efficacy and safety.

Material and methods: Electronic databases including PubMed, Embase, Wan Fang, VIP, CNKI and CBM database were researched from randomized controlled trials (RCTs) for redundant prepuce or phimosis. We conducted the direct and indirect comparisons by aggregate data drug information system (ADDIS) software. Moreover, consistency models were applied to assess the differences among the male circumcision practices, and the ranks based on probabilities of intervention for the different endpoints were performed. Node-splitting analysis was used to test inconsistency.

Results: Eighteen RCTs were included with 6179 participants. Compared with the conventional circumcision(CC), two new styles of circumcisions, the disposable circumcision suture device(DCSD) and Shang Ring circumcision(SRC), provided significantly shorter operation time[DCSD: standardized mean difference (SMD) = -20.60, 95% credible interval(CI) (-23.38, -17.82); SRC: SMD = -19.16, 95%CI (-21.86, -16.52)], shorter wound healing time [DCSD:SMD = -4.19, 95%CI (-8.24,-0.04); SRC: SMD = 4.55, 95%CI (1.62, 7.57);] and better postoperative penile appearance [DCSD: odds ratios odds ratios (OR) = 11.42, 95%CI (3.60, 37.68); SRC: OR = 3.85,95%CI (1.29, 12.79)]. Additionally, DCSD showed a lower adverse events rate than other two treatments. However, no significant difference was shown in all surgeries for 24 h postoperative pain score. Node-splitting analysis showed that no significant inconsistency was existed ($P > 0.05$).

Conclusions: Based on the results of NMA, DCSD may be a most effective and safest choice for phimosis and redundant prepuce. DCSD has the advantages of a shorter operation time, better postoperative penile appearance, fewer complication and shorter wound healing time. However, with the limitations of our study, additional multi-center RCTs are needed to evaluate the outcomes.

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1. Introduction

Redundant prepuce and phimosis are common symptoms in male adolescents who reached puberty stage, but the foreskin was still the glans penis, all the surround and cannot be turned on. For some men, excessive foreskin can cause inflammation and infection on glans penis. Thereby redundant prepuce and phimosis need removal through surgeries [1]. Dating back to more than 5000 years ago, male circumcision (MC), represented an effective strategy for those penile malformations, which has been performed with a prevalence of approximately 70% in the USA and 38.7% worldwide [1–3]. There are large volumes of published trials describing the benefits of MC, including easier urination, improved penile topical hygiene, increased sexual pleasure, and prevented urinary tract infections [4,5]. Additionally, it has been demonstrated that it can reduce sexually transmitted diseases (STDs), penile cancer and cervical cancer associated with harboring human papilloma virus [6,7].

There have been multiple methods of MC, such as sleeve circumcision, dorsal slit (DS), the suture less circumcision using tissue glue, Shang Ring circumcision (SRC) and a disposable circumcision suture device (DCSD). One of the most common surgeries is the conventional circumcision (CC) which has been recommended by World Health Organization (WHO) in 2008, including forceps guided, dorsal slit, and sleeve resection method [8]. Even the conventional circumcision as a golden standard surgery is widely performed in most MC programs. Unfortunately, it still has such disadvantages including adverse complications, inevitably suturing the incision, and cumbersome surgical procedure [9–11]. Moreover, those methods of the conventional circumcision require superior surgical technique to avoid the imperfect postoperative appearance, such as irregular hematoma [12]. In contrast, DCSD and SRC, two novel types of disposable circumcision devices, have substantial advantages which can simplify surgical process, shorten operative time, reduce adverse events, and achieve a satisfying appearance [12–16]. However, it is still existing controversy that MC practices are more clinically acceptable. Previous plenty researches have compared these surgeries in redundant prepuce and phimosis therapies, but the previous pairwise meta-analyses can not provide hierarchies of the comparative safety and efficacy in these treatments (CC, SRC and DCSD).

Therefore, we have collected high-quality randomized controlled trials (RCTs) in order to conduct an overall network meta-analysis for the comparative safety and efficacy in three treatments. Furthermore, we provide the hierarchies of the comparative operation time, intraoperative blood loss, 24 h postoperative pain score, wound healing time, the incidence of adverse events and the satisfaction on three interventions.

2. Materials and methods

2.1. Retrieval strategy

The systematic literature was performed according to the guidelines for preferred reporting items for systematic reviews and meta-analyses [17] (S1 file). We searched the electronic databases including PubMed, Embase, Wan Fang database, VIP database, Chinese National Knowledge Infrastructure (CNKI) and China Biology Medicine (CBM) database from their inception to December 30, 2016, collecting the eligible studies for treating redundant prepuce or phimosis without language limitation. The keywords or MeSH search headings were used as followed: “redundant prepuce,” “excess foreskin,” “phimosis,” “open surgical,” “conventional surgical,” “traditional surgical,” “disposable circumcision suture

device,” “circumcision stapler,” “DCSD,” “novel device,” “Shang Ring,” “ring device,” “Shang huan,” “disposable anastomosis device,” and “SRC.” In addition, a manual retrieval of references from related papers (reviews, meta-analyses and meeting reports) was performed. And thus, all relevant articles were reviewed to examine their eligibility. The procedure generated disagreements which were defused through discussion with all researchers.

2.2. Selection criteria

Studies we include were in line with the following criteria: (a) randomized controlled trials (RCTs); (b) the study included male patients with redundant prepuce or phimosis requiring circumcision; (c) studies involving the treatments among a disposable circumcision suture device (DCSD), conventional circumcision (CC) and Shang Ring circumcision (SRC); (d) full text available.

The following exclusion criteria were used: (a) summary, discuss theory, letters, case reports, comments, meta-analysis, review, and other types of research literature; (b) Duplicate publications and data were unavailable to odds ratios (OR) or standardized mean difference (SMD); (c) patients with genital malformations, urinary tract infection, coagulopathy, or diabetes.

2.3. Data extraction and quality assessment

The following data was extracted and recorded in predesigned forms from the eligible studies by two reviewers (CGH and PS) independently: the first author's name, publication year, study design, numbers of patients in each treatment group, ages of patients, the diagnostic criteria of patients, detail of interventions, follow-up period, and clinical outcome measurements. The outcomes included: (1) operation time; (2) wound healing time; (3) intraoperative blood loss; (4) 24 h postoperative pain score; (5) adverse event rate and (6) rate of satisfaction with postoperative penile appearance. During the procedure, if any disagreements have been generated, the studies would be discussed by all of us to determine whether included or not.

The assessment tool presented by Cochrane Handbook for Systematic Reviews Interventions version 5.1.3 was applied to evaluate the methodological quality of recruited clinical trials [18]. For included trials, the following criteria were evaluated for risk of bias: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias. Any discrepancies from this assessment would be defused through discussion or the third reviewer.

2.4. Data synthesis and analysis

Due to only three interventions (CC, SRC and DCSD) were included in our analysis, we can conduct the closed triangular circular network through both direct and indirect evidences. Moreover, to calculate the consistency of direct and indirect estimates, we performed node-splitting analysis based on ADDIS (Aggregate Data Drug Information System, version 1.16.8) [19, 20]. The result demonstrated that no statistical inconsistency existed in NMA when $P > 0.05$.

We firstly conducted pairwise meta-analyses for studies within DerSimonian-Laird random effects. The pair wise meta-analyses were performed through Stata software. The pooled estimates of odds ratios (ORs) or standardized mean difference (SMDs) and 95% credible interval (CI) of the endpoints were shown. The Mantel-Haenszel Chi-square based test and I² parameter test were used for evaluating the heterogeneity among RCTs [20]. For these estimates, the statistical significance should be tested using

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