INTRODUCTION

Chronic rhinosinusitis (CRS) is characterized by persistent inflammation of the sinus mucosa, which results in nasal congestion, postnasal drip, facial pressure, and decreased olfactory function [1,2]. Furthermore, it leads to chronic pain, depression, and social dysfunction, which impair quality of life [3]. Due to the high prevalence of CRS, the number of CRS cases that are intractable to medical treatment is also increasing. Accordingly, endoscopic sinus surgery (ESS) is becoming increasingly impor-
tant [4]. Although ESS is effective in resolving persistent CRS, local sinus inflammation may sometimes persist even after surgery, and surgical site adhesions and strictures may occur during the recovery process of the surgical site. This can slow recovery, potentially leading to the need for revision surgery [5,6]. To overcome this problem, steroid-impregnated spacers have been devised as a way to reduce local inflammation around the surgical area and prevent stenosis during postoperative recovery [7-23]. In this study, we reviewed the steroid-impregnated spacers reported to date and evaluated their effects on treatment outcomes using validated scales. Additionally, the rates of postoperative adverse outcomes such as adhesions, middle turbinate lateralization, the need for postoperative therapeutic interventions, scarring/synechia, and lysis of adhesions were compared with the control group. The goal of this meta-analysis of the literature on steroid-impregnated spacers was to comprehensively assess the efficacy of steroid-impregnated spacers for improving outcomes following ESS surgery. In addition, a subgroup analysis was performed to compare the effects of absorbable nasal dressing and drug-eluting sinus stents.

MATERIALS AND METHODS

Population, Intervention, Comparison, Outcomes and Study and selection criteria

The Population, Intervention, Comparison, Outcomes and Study (PICOS) of the study were as follows: (1) population: CRS patients who underwent functional ESS (primary or revision procedure); (2) intervention: steroid-impregnated packing, spacer, and stent; (3) comparison: packing, spacer, and stent without steroids; (4) outcomes: treatment and postoperative adverse outcomes; and (5) study design: no restrictions. Review articles, case reports, and studies with missing diagnostic data were excluded. Our institution does not require institutional review board approval for a systematic review and meta-analysis based exclusively on the published literature.

HIGHLIGHTS

- Steroid-impregnated spacers can effectively deliver a corticosteroid to the target site.
- Steroid-impregnated spacers improve the surgical outcomes of endoscopic sinus surgery patients, such as the degree of mucosal edema, ethmoid inflammation, crust formation, nasal discharge, polypoid changes, polyposis, Lund-Kennedy score, and the need for oral steroid usage.
- Steroid-impregnated spacers reduce postoperative adhesions, middle turbinate lateralization, scarring/synechia, and the need for postoperative therapeutic interventions.

Search strategy

The following databases were searched from inception to November 2022: PubMed, Scopus, Embase, the Web of Science, Google Scholar, and the Cochrane database. Search terms and queries are listed in Supplementary Table 1. Two independent researchers (DHK and MAB) reviewed and screened the titles and abstracts of all potentially eligible studies and excluded those unrelated to our topic. If the abstract alone was not sufficient for determining whether a study was suitable for inclusion, the full text was checked. If the opinions of the two researchers differed, study eligibility was decided via discussion with a third reviewer (SWK). A flowchart of the study selection process is presented in Fig. 1. The study protocol is registered on Open Science Framework (https://osf.io/fhc42/).

Data extraction and risk of bias assessment

We extracted the following data from eligible studies: the number of patients, scale used for assessing endoscopic findings, incidence of postoperative adverse events (adhesions, middle turbinate lateralization, polyposis, and the need for postoperative therapeutic intervention), and P-values for comparisons between treatment (steroid-impregnated spacers) and control (conventional management) groups. The studies were organized using a standardized format [24,25]. Outcome measures were
The LK and POSE scores were significantly lower in the steroid-regression analyses for all outcomes, publication bias was not the bias assessment results are presented in Supplementary Table 2, and study characteristics are listed in Supplementary Tables 2, and that the data are normally distributed. For outcomes when significant heterogeneity among outcomes was found (I² ≥50), a fixed-effects model using the inverse variance approach was employed, in showing no significant heterogeneity (I² <50), a fixed-effects model using the inverse variance approach was employed, in which it is assumed that all studies are based on the same population. Sensitivity analyses were also conducted to assess the effect of each study on the overall results of the meta-analysis.

RESULTS

In total, 16 of the 1,274 identified articles were included. The study characteristics are listed in Supplementary Tables 2, and the bias assessment results are presented in Supplementary Tables 3. Because the number of included studies was not sufficient (<10) to generate an adequate funnel plot or perform advanced regression analyses for all outcomes, publication bias was not evaluated.

Treatment and control group scores
The LK and POSE scores were significantly lower in the steroid-impregnated spacer group at 2–3 weeks (−1.1495; 95% CI, −1.8207 to 0.4783; F=87.8%; P=0.0008 and −1.7656; 95% CI, −3.0236 to 0.5075; F=91.8%; P=0.0060, respectively) and 2–3 months postoperatively (−0.9597; 95% CI, −1.6491 to 0.2702; F=90.2%; P=0.0064 and −0.9602; 95% CI, −1.6442 to 0.2762; F=91.0%; P=0.0059, respectively) than in the control group (Fig. 2A-D).

The degree of postoperative crusting at 2–3 weeks postoperatively (−0.4188; 95% CI, −0.6575 to 0.1802; F=0.0%; P=0.0006), nasal discharge at 2–3 months postoperatively (−0.3851; 95% CI, −0.6628 to 0.1074; F=14.5%; P=0.0066), mucosal edema at 2–3 weeks (−0.3609; 95% CI, −0.5987 to 0.1231; F=0.0%; P=0.0029) and 2–3 months postoperatively (−0.4290; 95% CI, −0.7073 to 0.1507; F=12.8%; P=0.0025), ethmoid inflammation at 1 month postoperatively (−0.5080; 95% CI, −0.7109 to 0.3051; F=0.0%; P<0.0001), polyposis changes at 1 month (0.3263; 95% CI, 0.2415; 0.4408; F=0.0%; P<0.0001) and 2–3 months (0.3021; 95% CI, 0.1697–0.5378; F=0.0%; P<0.0001), polyposis at 2–3 months postoperatively (−0.5226; 95% CI, −0.8958 to 0.1493; F=28.6%; P=0.0061), and the need for oral steroid use (0.4975; 95% CI, 0.3312–0.7471; F=0.0%; P=0.0008) were significantly lower in the steroid-impregnated spacer group than in the control group. However, there were no significant between-group differences in crusting at 2–3 months postoperatively (−0.2041; 95% CI, −0.4791 to 0.0709; F=0.0%; P=0.1458), nasal discharge at 2–3 weeks postoperatively (−0.2106; 95% CI, −0.4791 to 0.0709; F=0.0%; P=0.0001), polyposis at 2–3 weeks postoperatively (−0.5226; 95% CI, −0.8958 to 0.1493; F=28.6%; P=0.0061), and the need for oral steroid use (0.4975; 95% CI, 0.3312–0.7471; F=0.0%; P=0.0008) were significantly lower in the steroid-impregnated spacer group than in the control group. However, there were no significant between-group differences in crusting at 2–3 months postoperatively (−0.2041; 95% CI, −0.4791 to 0.0709; F=0.0%; P=0.1458), nasal discharge at 2–3 weeks postoperatively (−0.2106; 95% CI, −0.4791 to 0.0709; F=0.0%; P=0.0001), polyposis at 2–3 weeks postoperatively (−0.2750; 95% CI, −0.5629 to 0.0128; F=0.0%; P=0.0611) (Fig. 2E-P).

Postoperative adverse outcomes: comparison between the treatment and control groups
The steroid-impregnated spacer group showed significantly lower rates of middle turbinate lateralization (0.3887; 95% CI, 0.1835–0.8233; F=0.0%; P=0.0136), non-medical or -surgical postoperative therapeutic interventions (0.3358; 95% CI, 0.2505–0.4501; F=38.2%; P<0.0001), and lysis of adhesions (0.3259; 95% CI, 0.2350–0.4519; F=41.0%; P=0.0001) than the control group. Although the rates of adhesion at 2 weeks (0.7788; 95% CI, 0.2589–2.3422; F=0.0%; P=0.6563), and scarring/synechia at 2–3 weeks (−0.2752; 95% CI, −0.5697 to 0.0193; F=0.0%; P=0.0670) did not differ between the groups postoperatively, there was a difference in adhesions at 1 month (0.3179; 95% CI, 0.1911–0.5290; F=0.0%; P<0.0001) and both adhesions (0.2882; 95% CI, 0.1451–0.5724; F=0.0%; P=0.0004) and scarring/synechia (−0.3326; 95% CI, −0.6225 to 0.0426; F=0.0%; P=0.0246) at 2–3 months postoperatively (Fig. 3).
Fig. 2. Severity of postoperative adverse outcomes based on endoscopic examinations: comparison between the treatment and control groups. The Lund-Kennedy score at 2–3 weeks (A), and 2–3 months (B), perioperative sinus endoscopy score at 2–3 weeks (C) and 2–3 months (D).

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difference between the two groups regarding adhesions (2–3 weeks) \((P=0.5807)\), polypoid change (2–3 weeks) \((P=0.7174)\), and polypoid changes (2–3 months) \((P=0.4618)\) (Supplementary Table 4).

Sensitivity analyses

Sensitivity analyses were performed by repeating the meta-analysis several times while omitting one study on each occasion.
Fig. 2. (Continued) And 2–3 months (J), ethmoid inflammation at 1 month (K), polyposis at 2–3 weeks (L) and 2–3 months (M).

The results were consistent with those reported above.

**DISCUSSION**

We performed a meta-analysis of the efficacy of steroid-impregnated spacers for CRS patients undergoing ESS. Steroid-impregnated spacers reduced the LK and POSE scores and the incidence of postoperative complications, especially after 2–3 months. The steroid-impregnated spacers in this study can be divided into absorbable nasal dressings and drug-eluting sinus stents. The steroids used included triamcinolone, budesonide, betamethasone, mometasone furoate, and fluticasone propionate. In most studies, steroid-impregnated spacers were associated with better postoperative outcomes. Important postoperative parameters such as adhesion, synechia, and polypoid changes showed no significant differences between the absorbable nasal dressing and drug-eluting sinus stent groups. In this study, the number of included studies,
Fig. 2. (Continued) Polypoid changes at 1 month (N) and 2–3 months (O), and the need for oral steroid use (P). SD, standard deviation; SMD, standardized mean difference; CI, confidence interval.

the number of patients included, and analysis outcome items were analyzed in more than twice as many studies as in the previously reported literature [27-29]. Therefore, it was possible to obtain improved analytical power and reliability for the analyzed items. In addition, the analysis of the effects in absorbable steroid-soaked nasal spacer and steroid-eluting sinus stent groups, which are known to show greater efficacy than the control group in individual studies, demonstrated that there was no significant difference in the effect between these two treatment groups.

Evidence is accumulating that steroid-impregnated spacers have a direct anti-inflammatory effect on inflamed sinus mucosa, and are also effective in cases of ESS-induced tissue disruption [30,31]. Furthermore, since it is difficult to precisely reach the desired site of application for topical corticosteroids, steroid-impregnated spacers could potentially be more effective than topical preparations [16]. Steroid-impregnated spacers are thought to enhance healing after surgery due to their anti-inflammatory role resulting from the steroid effects, and to prevent adhesion and synechia through the effect of the spacer [15,17]. In the sinus mucosal healing process, the first stage (1–10 days) is domi-
Fig. 3. Postoperative adverse outcomes: comparison between the treatment and control groups. Middle turbinate lateralization at 1 month (A), adhesions at 2 weeks (B), 1 month (C), and 2–3 months (D). (Continued to the next page)
nated by blood crusting without significant changes in the underlying residual mucosa, and the second stage (up to 30 days) is dominated by edematous edema of the residual mucosa [32]. Obstructive edema, which is common in this second phase, responds well to topical steroids [32]. This might be the basis for the significant results observed in follow-up observations for more than 1 month, although several items on surgical outcomes or postoperative complication may not have shown statistically significant differences compared to the control group at 2–3 weeks postoperatively.

Although absorbable nasal packing may have a shorter effect duration than drug-eluting sinus stents, the overall effect is nonetheless similar; however, additional research is needed because the number of comparative studies is small. In terms of price, steroids such as triamcinolone, dexamethasone, and betamethasone cost <$10 USD per dose, whereas Nasopore, an absorbable nasal packing used in many studies, costs $130 USD (for two 8-cm pieces). PROPEL sinus implants, which are used as drug-eluting sinus stents, cost $1,390 USD (for two implants). It is necessary to consider cost-effectiveness when selecting a ste-
Steroid-impregnated spacer.
This meta-analysis had several limitations. First, variables such as patients’ baseline characteristics, the spacer types, and intervention period could have affected the results. Furthermore, preoperative medication, postoperative patient management, and patient compliance may have varied among the studies, and controlling for these variables is beyond the scope of a meta-analysis. More clinical trials using similar treatment regimens would be needed to overcome this issue. Second, various steroid drugs and spacers were used. To address this, we conducted a subgroup analysis of absorbable nasal dressings and drug-eluting sinus stents. Third, the final outcomes in most studies were evaluated within 3 months; however, a longer follow-up (e.g., 6 months) may be required in some patients. Therefore, well-designed large-scale studies with long-term follow-up are needed. Steroid-impregnated spacers will be useful for CRS patients, as they improve the surgical outcomes of ESS patients and reduce the incidence of postoperative complications.

CONFLICT OF INTEREST
Sung Won Kim and Do Hyun Kim are editorial board members of the journal but were not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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SUPPLEMENTARY MATERIALS
Supplementary materials can be found online at https://doi.org/10.21053/ceo.2022.01718.

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