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META-ANALYSIS

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Is drug-induced sleep endoscopy associated with better outcomes after soft tissue surgery for sleep apnea? A systematic review and meta-analysis

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Abstract

Objectives: The aim was to estimate the effect of drug-induced sleep endoscopy (DISE) on surgical outcomes after soft tissue surgery for obstructive sleep apnea (OSA).

Design and Setting: Systematic review and meta-analysis.

Participants: Adult patients with OSA and candidates for soft tissue surgery, with and without preoperative DISE, were included.

Main Outcomes Measures: A systematic literature search of Medline, Web of Science, and Cochrane databases was performed from inception to December 31, 2021. Studies directly comparing patients with and without preoperative DISE were included. Success rate, change in apnea-hypopnea index (AHI), change in minimum SpO_2 and change in Epworth Sleepiness Scale (ESS) score were extracted. Random-effect models were used to pool estimates.

Results: Seven out of 619 articles were included, representing 791 patients (389 in the DISE group and 402 in the no DISE group). DISE was neither associated with a higher success rate (pooled OR 1.34, 95% CI 0.69–2.59, $p = 0.39$) after soft tissue surgery for OSA, nor a significant change in AHI (−4.69 events/hour, 95% CI −11.10 to 1.72, $p = 0.15$), minimal SpO_2 (mean increase of 2.02%, 95% CI −0.26 to 4.29, $p = 0.08$) and ESS (mean difference of 1.29, 95% CI −0.48 to 3.05, $p = 0.15$) when compared to patients without preoperative DISE.

Conclusions: Soft tissue surgery does not give better results after DISE compared to when DISE is not performed. However, given the overall low level of evidence of included studies, future well-conducted studies should confirm or overturn these results and clarify the added value of DISE.

KEYWORDS
drug induced sleep endoscopy, meta-analysis, sleep apnea, surgery

1 | INTRODUCTION

Obstructive sleep apnea (OSA) is highly prevalent, affecting up to 49% of men and 23% of women in a general population setting aged above 40 years.[1] OSA is characterised by repeated episodes of collapse of upper airway and the most effective therapies to date rely on nocturnal positive airway pressure (PAP) and on mandibular advancement devices (MAD) under some circumstances. Both are suspensive treatments, and their efficacy mainly depends on the patient's long-term adherence. Hence, in case of PAP and/or MAD failure or

refusal, surgery can be considered as an alternative in treating OSA, its great advantage being its permanent effectiveness, even partial.[2] While maxillomandibular surgery is associated with excellent outcomes regarding OSA,[3] results of soft tissue surgeries are more mitigated.[4]

In order to improve patient selection and thus increase surgical success after soft tissue surgery for OSA, drug-induced sleep endoscopy (DISE) has been developed.[5] DISE aims at identifying the precise site of obstruction(s), hence helping in the choice of soft tissue surgery. DISE has been shown to identify the sites of obstruction compared to the awake Muller's manoeuver more accurately.[6] However, and despite that DISE changes surgery plan in up to 64% compared to surgical planning based on awake clinical examination,[7,8] uncertainty remains regarding its efficacy on surgical outcomes.[9] In fact, conflicting results regarding the effect of DISE on surgical outcomes have been reported, and the largest study on the field including more than 300 patients in seven centres worldwide reported that DISE was not associated with improved outcomes.[10]

To clarify in which extent performing a DISE pre-operatively is associated with better surgical outcomes after soft tissue surgery for OSA, a systematic review and meta-analysis of studies evaluating outcomes after soft tissue surgery for OSA, with versus without pre-operative DISE was conducted.

Key Points

- It is unclear whether drug-induced sleep endoscopy (DISE) is associated with better surgical outcomes after soft tissue surgery for obstructive sleep apnea (OSA).
- We performed a systematic review and meta-analysis evaluating the effect of DISE on surgical outcomes, and seven studies including 791 patients were included.
- DISE was neither associated with an improved success rate after surgery nor with an improved apnea-hypopnea index, minimal SpO_2 or Epworth Sleepiness Scale score.
- This study does not support the use of DISE in order to improve surgical outcomes after soft tissue surgery for OSA.
- However, the low level of evidence of included studies as the high heterogeneity of the literature underlines the need for further well-conducted studies evaluating the added value of DISE.

2 | METHODS

2.1 | Reporting and registration

This systematic review and meta-analysis follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines.[11,12] The study protocol was registered on the international prospective register of systematic review (PROSPERO, https://www.crd.york.ac.uk/prospero/) under the identification number CRD42021295882.

2.2 | Information source and search strategy

Two authors (QL and RB) carried out a literature search in the Medline, Web of Science, and Cochrane databases, without language restriction, from inception to December 31, 2021, using the following search terms: DISE, drug-induced sleep endoscopy, and sleep endoscopy.

2.3 | Selection process and eligibility criteria

After removal of inadequate publication types (review, case report or opinion), two reviewers (QL and RB) independently screened articles and assessed them for eligibility. Potential conflicts were resolved by discussion with a third author (MB). Inclusion criteria were: observational study or randomised controlled study; including adults patients with OSA and candidate for soft tissue sleep surgery given inefficiency, failure, or refusal of primary treatments of sleep apnea (i.e., PAP or MAD); studies in which it was possible to identify outcomes for patients with preoperative DISE and for those without and reporting at least change in apnea-hypopnea index (AHI) and/or success rate (with a clear definition of success). Exclusion criteria were paediatric population, skeletal surgery, hypoglossal nerve stimulation, and transcutaneous electrical stimulation.

2.4 | Data collection

Using a standardised extraction form, the following variables were extracted when available: author; year of publication; country of origin; study design; years of inclusion; number of patients (overall and in each group, i.e., 'DISE group' versus 'no DISE group'); number of males and females (overall and in each group); the type of sleep device used (polysomnography or home sleep apnea test); surgical indication; surgical technique; the reason to perform or not DISE preoperatively; the absolute number of success, and the postoperative reassessment period. When available, mean, median, minimum, maximum and standard deviation were extracted overall and for each group (i.e., 'DISE group' versus 'no DISE group') for the following variables, before and after surgery: age; body mass index (BMI); AHI; minimal SpO_2; and the Epworth sleepiness score (ESS).

2.5 | Risk of bias of included studies

The risk of bias was assessed using the Cochrane Risk of Bias tool 2.0 for randomised controlled trial[13] and ROBINS-I for assessing risk of bias in non-randomised intervention studies.[14]

2.6 | Statistical analyses

In all analyses, the exposure was the realisation of preoperative DISE. A first analysis was performed considering the binary outcome 'success rate'. Odds ratio (OR) and 95% confidence intervals (CI) were computed for each study and a random-effect model was used to pool estimates. Then, analyses of continuous outcomes were performed with the change in the considered outcome between postoperative and preoperative as the outcome. Standard deviation of change was estimated following the Cochrane handbook recommendations.[15] Random-effect models were used to pool estimates. In all analyses, the I^2 statistic was used to assess heterogeneity and a value >50% was considered as high heterogeneity.[16] Risk of publication bias was evaluated using funnel plots, and asymmetry was tested using Egger's test. Finally, to identify the impact of each individual study, we performed an influence analysis in which one study at a time is omitted and pooled estimates are recalculated.

All analyses were performed using the R software version 3.6.2 (www.r-project.org) and using the '*meta*' and '*metafor*' packages.

3 | RESULTS

3.1 | Study selection

As illustrated in the flow chart (Figure 1), 619 articles were identified, of which 137 were neither a cohort study nor a randomised trial. Of the 482 remaining articles, 7 were included in the meta-analysis, including six observational studies[10,17–21] and one randomised trial.[22] These seven articles represent 791 patients, 389 in the DISE group and 402 in the no DISE group. After reviewing the bibliography of the considered studies, no additional article was included. All the seven articles were published between 2015 and 2021, and all included patients that have been treated from 2008 up to the end of 2019.

3.2 | Study characteristics

Polysomnography was used in five studies, while Chen et al.,[17] used both polysomnography and home sleep apnea testing (HSAT) and Iannella et al.[22] exclusively used HSAT. As presented in Table 1, the number of included patients ranged from 47 to 326. Of note, in the study by Huntley et al.,[20] 33 patients who beneficiated from upper airway stimulation were excluded from the current analysis. In all studies, mean age was between 41.8 and 50.4 years old, and mostly included men (ranging from 70.3% to 94%). BMI mostly ranged between 25 and 30 kg/m^2.

DISE was performed with propofol alone in four studies,[17,18,20,21] with various drugs in another (propofol alone, propofol + remifentanil or dexmetidine + remifentanil)[19] and one centre included in the multicentric study from Pang et al. performed dexometidine-DISE.[10] The VOTE classification[23] was used in five studies,[10,17,19,20,22] a

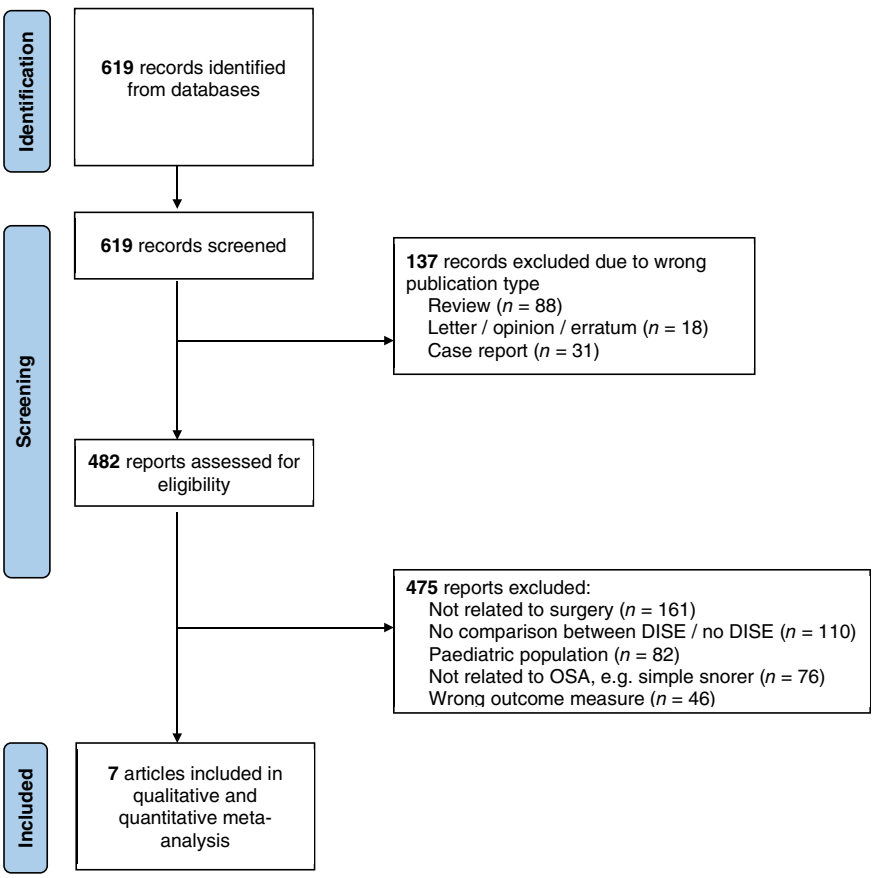

FIGURE 1 Flow chart of study selection

TABLE 1 Studies' characteristics

			DISE group				No DISE group				
	Country	*N* total	*N* total	*N* men (%)	Mean age ± SD	Mean BMI ± SD	*N* total	*N* men (%)	Mean age ± SD	Mean BMI ± SD	Time to reassessment, months
Chen, 2021[17]	Taiwan	47	25	21 (84)	47 ± 9.7	27.5 ± 4	22	16 (72.7)	43.8 ± 13.4	28.4 ± 4.7	3 (minimum)
Golbin, 2015[18]	USA	104	64	45 (70.3)	49 (*SD missing*)	NA	40	29 (72.5)	50.4 (*SD missing*)	NA	3 (minimum)
Ha, 2020[19]	South Korea	95	48	42 (87.5)	41.8 ± 12.2	26.3 ± 3.2	47	40 (85.1)	44.3 ± 12.1	25.3 ± 3.2	3 (minimum)
Huntley, 2017[20]	USA	54	17	NA	NA	NA	37	29 (78.4)	47.2 ± 9.6	30.4 ± 4.9	NA
Iannella, 2021[22]	Italy	92	42	37 (88.1)	47.9 ± 12.9	27.3 ± 3.3	50	47 (94.0)	45.5 ± 13.8	28.1 ± 3	6
Pang, 2016[21]	Multicentre[a]	73	23	NA	NA	NA	50	NA	NA	NA	3–30
Pang, 2020[10]	Multicentre[b]	326	170	NA	44.2 ± 14.3	27.6 ± 4.6	156	NA	46.4 ± 10.1	28.1 ± 3.9	8.2 (mean)

Abbreviations: BMI, body mass index; DISE, drug-induced sleep endoscopy; NA, not available.
[a]Singapore and Italy.
[b]Singapore, Canada, India, Spain, Poland, Israel, and Korea.

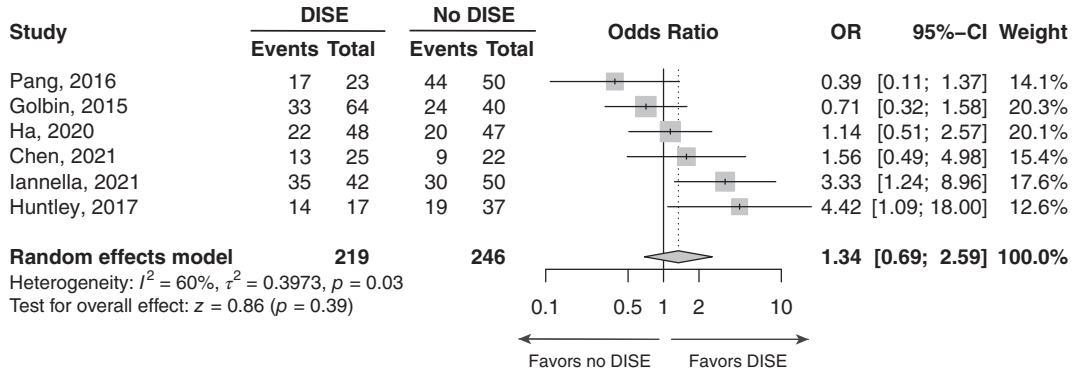

FIGURE 2 Forest plot of success rate according to DISE or no DISE preoperatively. CI, confidence interval; DISE, drug-induced sleep endoscopy; OR, odd ratio

VOTE-adapted classification was used in one study,[21] and the classification system used was not described in the last study.[18]

In all studies, surgery followed a previous treatment (PAP and/or mandibular advancement device) that failed or was not tolerated. Inclusion and exclusion criteria for each study, as the type of surgery performed, are detailed in Table S1. Indications for performing preoperative DISE for each included study are detailed in Table S2. DISE was performed in case of discrepancies between the Mueller manoeuver and OSA severity in two studies, and was implemented in clinical practice in two other studies. DISE was randomised in one study, and was at surgeon's discretion in two.

Overall risk of bias of included studies was moderate or serious, the main domain of concern being controlling for confounding, as presented in Figure S1.

3.3 | Meta-analysis results

3.3.1 | Success rate

Six articles reported success rates, representing 465 patients (219 in the DISE group and 246 in the no DISE group). In five articles,[17,19–22] success was defined according to the Sher's criteria (a decrease in AHI >50% and AHI <20 events/hour)[24] and one used a slightly modified definition of success rate (a decrease in AHI >50% and AHI <15 events/hour).[18]

Four articles reported non-significant associations between DISE and success rate,[17–19,21] and two found a significant association between DISE and success rate (OR 4.42 and 3.33, corresponding 95% CI being 1.09–18.0 and 1.24–8.96).[20,22] As presented in Figure 2,

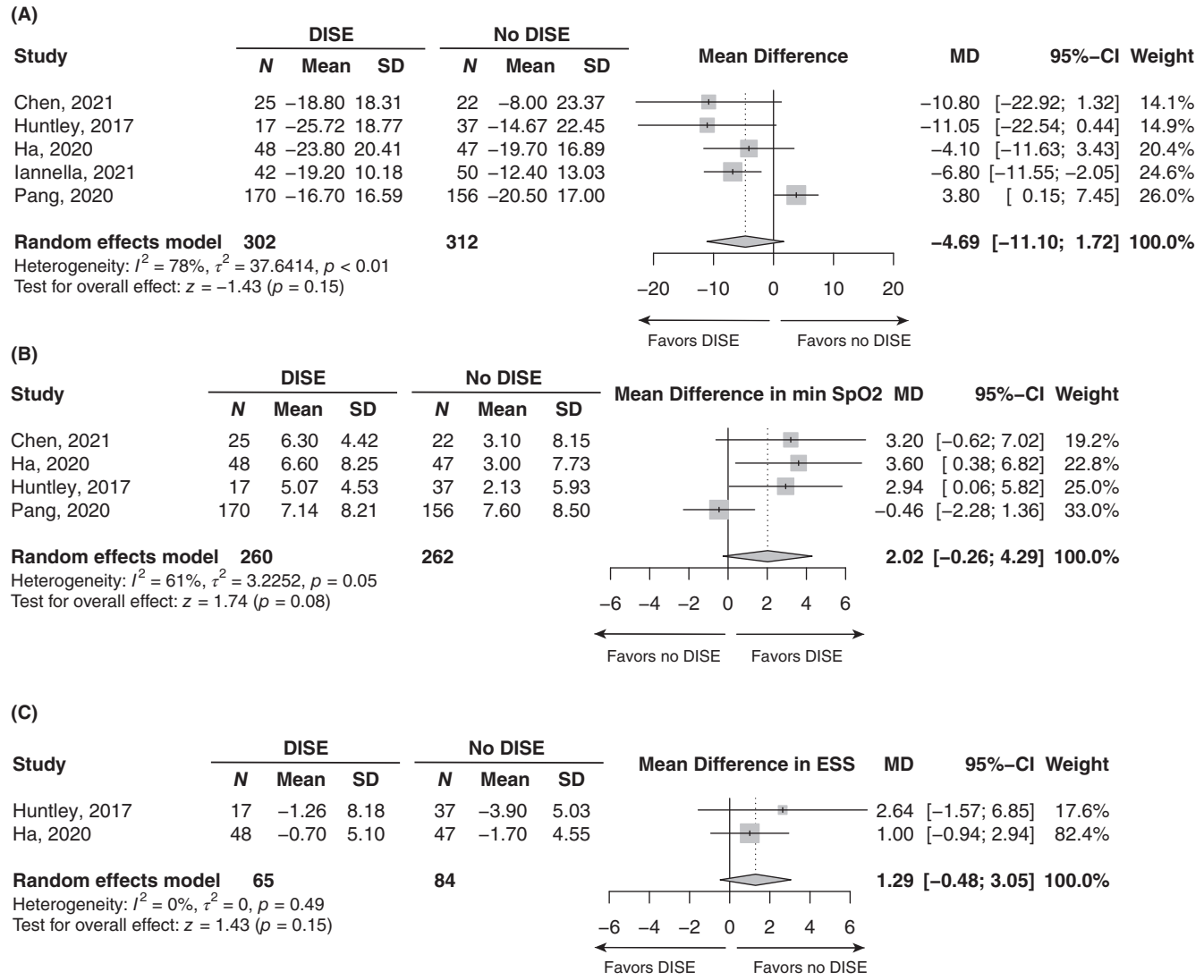

FIGURE 3 Forest plot of (A) AHI, (B) minimal SpO_2 and (C) Epworth Sleepiness Score changes according to DISE or no DISE preoperatively. AHI, apnea-hypopnea index; CI, confidence interval; DISE, drug-induced sleep endoscopy; ESS, Epworth Sleepiness Score; MD, mean difference

pooled analysis revealed no significant associations between DISE and success rate (pooled OR 1.34, 95% CI 0.69–2.59, $p = 0.39$). Significant between-studies heterogeneity was found (I^2 60%, $p = 0.03$).

3.3.2 | Apnea-hypopnea index

Five articles reported changes in AHI, pre and postoperatively according to the realisation or not of a pre-operative DISE.[10,17,19,20,22] They represented 614 patients overall, 302 in the DISE group and 312 in the no DISE group. In all studies, mean postoperative AHI was lowered, reductions ranging from −8 to −25.7 events/hour compared to preoperative AHI. The mean difference between 'DISE' versus 'no DISE' groups was not significant in three studies.[17,19,20] A significant difference was found in favour of the 'no DISE' group in one study (a greater reduction of 3.8 events/hour compared to the 'DISE group')[10] and a significant difference in favour of the 'DISE group' was found in another study (greater reduction of AHI of 6.8 events/hour in the 'DISE group' compared to the 'no DISE group').[22] As presented in Figure 3A, the pooled mean difference found a non-significant lower AHI in favour of the DISE group (−4.69 events/hour, 95% CI −11.10 to 1.72, $p = 0.15$). A significant heterogeneity was found (I^2 78%, p < 0.01).

3.3.3 | Minimal SpO_2

Four articles reported changes in minimum SpO_2, representing 522 patients.[10,17,19,20] Two articles found a non-significant association between DISE and change in minimum SpO_2[10,17] while two found a significant association in favour of the 'DISE group' (greater increase in minimal SpO_2 of 2.94% and 3.60% in the 'DISE group' when compared to the no 'DISE group').[19,20] However, the pooled mean difference was not significant (greater increase in minimal SpO_2 of 2.02% in favour of

the 'DISE group', 95% CI −0.26 to 4.29, $p = 0.08$) as presented in Figure 3B. Borderline heterogeneity was found (I^2 61%, $p = 0.05$).

3.3.4 | Epworth sleepiness score

Two articles reported on the change in the ESS, including 149 patients (65 with DISE and 84 without).[19,20] None of them found a significant reduction of postoperative ESS in favour of a group, and the pooled mean difference change in ESS was 1.29 (95% CI −0.48 to 3.05, $p = 0.15$, Figure 3C). No heterogeneity was noted (I^2 0%, $p = 0.49$).

3.4 | Risk of publication bias

No publication bias was found neither for the analysis of success rate (no asymmetry in funnel plot, $p = 0.55$) nor for the analysis of change in AHI ($p = 0.17$). A borderline asymmetry in the funnel plot was found for the analysis of change in minimal SpO_2 ($p = 0.05$). Test was not performed for the analysis of change in ESS given the small number of studies ($N = 2$).

3.5 | Influence analyses

Regarding success rate, omitting studies one at a time would not have impacted pooled OR and 95% CI for success rate. For AHI and minimal SpO_2 changes, only omitting the study by Pang et al.[10] would have changed the results in favour of DISE. These results are presented in Figure S2.

4 | DISCUSSION

From this systematic review and meta-analysis, we found that DISE was not associated with a higher success rate after soft tissue surgery for OSA when compared to patients without pre-operative DISE. Moreover, DISE was not associated with better outcomes regarding change in AHI, minimal SpO_2 nor ESS. Significant between-studies heterogeneity was found.

Several hypotheses can be raised regarding the lack of association between preoperative DISE and better surgical outcomes. First, one can assume that once a main obstruction site is identified, this one only will be treated, neglecting potential secondary obstruction sites resulting in contrasted surgical outcomes. Contrariwise, some authors do not perform preoperative DISE and systematically achieve multilevel surgery addressing the two main sites of obstruction (i.e., the velum and the tongue).[25]

Second, some results are mainly drove by the study by Pang et al.[10] By omitting this study, changes in AHI and minimal SpO_2 were in favour of performing DISE. However, these results are to be taken with caution given that the study by Pang et al. has numerous strengths over other included studies, being the largest, including patients in seven centres worldwide and controlling for potential confounders.

Third, DISE is generally rated using the VOTE classification,[23] yielding a relative homogeneity across centres. However, assessment of obstructive sites during DISE is partly subjective and may be subject to misclassification bias, resulting in discrepancies between different observers. Indeed, extremely varying interrater reliability has been reported but it is generally low to moderate,[26–28] and low agreement has been reported in non-experienced practitioners.[29] Therefore, misclassification of the site or type of collapse and neglect of secondary obstruction site may lose the advantage offered by DISE over awake clinical examination in determining the site of obstruction, resulting in unimproved surgical outcomes.

Fourth, it can be assumed that, while DISE allows for a better understanding of the underlying obstruction sites in subjects with OSA, not observing an improved operative efficiency after DISE may reflect the globally limited efficiency of these surgical techniques in terms of AHI reduction and success rate, independently from performing DISE or not.

Finally, those results may highlight an indication bias, that is, inadequate selection of surgical procedure after DISE. Given that precise indication for each surgical procedure based on DISE findings was mainly not available in included studies, it is not possible to assess in which extent DISE precisely drove surgical indications. Indeed, there is a discrepancy between the data of the literature, often retrospective, which underlines the numerous benefits of DISE in the planning of the most personalised, effective and least morbid surgical gesture (i.e., decreased utilisation of multilevel procedure)[28,30,31] and our results. In this regard, the lack of association between DISE and improved surgical outcomes may reflect inadequate surgical indication following DISE, underlining the need for global agreement on which surgery should be performed based on DISE findings.

If confirmed, our results imply that the role of DISE in clinical practice is not entirely elucidated yet. Those results may underline that the surgical and therapeutic implications of DISE are not as clearly established as its diagnostic value. A risk of over or undertreatment depending on the obstructive sites identified exists and surgeons should strive to pay thorough attention to the conclusions they draw from DISE in terms of operative indications. Further, the role of DISE may not lie in directing surgical indication but in identifying surgical contra-indication, such as complete concentric collapse in hypoglossal stimulation.[32] It can also be interpreted that, considering that there has been no consensus on DISE indication since its introduction[33] and given that DISE does not seem to be associated with better surgical outcomes, DISE might be optional as a first-line setting before OSA surgery in case of PAP/MAD failure, as advocated by some authors.[34] Hence, the added value of DISE may lie in patients in whom a first upper airway surgery for OSA has failed, and the utility of DISE in this scenario should be investigated. Of note, all associations and confidence intervals were in favour of DISE, but none reached statistical significance. This may suggest that the current meta-analysis lacks power and that the benefits of DISE on the considered outcomes may be significant with an increased sample size.

Several limitations should be considered. First, the overall quality of evidence remains low since included studies are of limited level of evidence, and all had very limited follow-up. Importantly, only one study controlled for confounders with minimal adjustments (age, sex and BMI),[10] raising the issue of residual confounding. Given this global low quality of evidence in the field, the current meta-analysis also underlines the need for further well-conducted cohort studies or randomised controlled studies to confirm or overturn our findings. Second, although not systematically significant, between-studies heterogeneity was globally high. Third, several important outcomes are missing from included studies, since no study reported on blood pressure reduction for instance, or on patient-centred outcomes such as quality of life or snoring. Only two studies assessed changes in ESS. Importantly, none reported changes in hypoxic burden or time with SpO_2 < 90%, which seem to be strongly associated with incident cardiovascular disease and mortality.[35] Fourth, while this meta-analysis evaluates the impact of DISE on surgical outcomes, surgical procedures are heterogeneous, both inter and intra-studies. However, it is likely that this bias is non-differential among included studies, and between studies heterogeneity is accounted for using random-effect modelling. Fifth, although indication for performing DISE was detailed, it cannot be ruled out that patients with obvious level of obstruction (i.e., grade 4 tonsils) on clinical examination were never offered DISE, hence biasing results since these patients have favourable outcomes.[36] Finally, many different surgical procedures were performed in included studies, all with various reported efficacy. However, the lack of details regarding indications and target population precludes analysing efficacy of each different procedure as taking into account the type of surgery in main analyses.

In conclusion, DISE does not seem to improve surgical outcomes after soft tissue surgery for OSA. However, given the overall low level of evidence of included studies and the high heterogeneity of the published literature, our results underline the need for future well-conducted studies to confirm or overturn these findings in order to clarify the place of DISE in the armamentarium of sleep surgeons.

AUTHOR CONTRIBUTIONS

Concept and design: all authors. Acquisition, analysis, or interpretation of data: Quentin Lisan, Robin Baudouin. Drafting of the manuscript: Quentin Lisan and Robin Baudouin. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: Quentin Lisan.

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CONFLICT OF INTEREST

None reported.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

Data Availability Statement: data may be made available on request.

ETHICS STATEMENT

There is no ethic statement given the type of study (meta analysis), which does not require ethic committee.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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