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 SpO2 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 (\(-4.69 \text{ events/hour}, 95\% \text{ CI} \) 11.10 to 1.72, \( p = 0.15 \)), minimal SpO2 (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. 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 endos-
copy (DISE) has been developed.\(^5\) DISE aims at identifying the precise
site of obstruction(s), hence helping in the choice of soft tissue sur-
gery. DISE has been shown to identify the sites of obstruction com-
pared 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, conflict-
ing 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 out-
comes after soft tissue surgery for OSA, with versus without pre-
operative DISE was conducted.

## 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 num-
ber 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: obser-
vational 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 out-
comes for patients with preoperative DISE and for those without and
reporting at least change in apnea-hypopnea index (AHI) and/or suc-
cess 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 ori-
gin; 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 stan-
dard 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. Random-effect models were used to pool estimates. In all analyses, the I² statistic was used to assess heterogeneity and a value >50% was considered as high heterogeneity.

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 and one randomised trial. 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. used both polysomnography and home sleep apnea testing (HSAT) and Iannella et al. 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., 33 patients who benefited 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/m².

DISE was performed with propofol alone in four studies, with various drugs in another (propofol alone, propofol + remifentanil or dexmedetomidine + remifentanil) and one centre included in the multicentric study from Pang et al. performed dexmedetidine-DISE. The VOTE classification was used in five studies,

FIGURE 1 Flow chart of study selection
VOTE-adapted classification was used in one study, and the classification system used was not described in the last study.

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, success was defined according to the Sher’s criteria (a decrease in AHI >50% and AHI <20 events/hour) and one used a slightly modified definition of success rate (a decrease in AHI >50% and AHI <15 events/hour) in other studies. DISE was randomised in one study, and was at surgeon’s discretion in two.

Four articles reported non-significant associations between DISE and success rate, 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). As presented in Figure 2,
However, the pooled mean difference was found to be non-significant in favour of the ‘DISE’ group compared to the ‘no DISE’ group. As presented in Figure 3A, the pooled mean difference was found to be non-significant in favour of the ‘DISE’ group compared to the ‘no DISE’ group.

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. 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. 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’) 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’). As presented in Figure 3A, the pooled mean difference was found to be non-significant in favour of the ‘DISE’ group compared to the ‘no DISE’ group.

3.3.3 | Minimal SpO2

Four articles reported changes in minimum SpO2 representing 522 patients. Two articles found a non-significant association between DISE and change in minimum SpO2 while two found a significant association in favour of the ‘DISE group’ (greater increase in minimum SpO2 of 2.94% and 3.60%) and a significant difference in favour of the ‘DISE group’ when compared to the ‘no DISE group’. However, the pooled mean difference was not significant (greater increase in minimal SpO2 of 2.02% in favour of...
Therefore, mis-
and our
Hence, the added value of DISE may lie in patients in
None of them found a significant 
and given that DISE does not seem to be associated with better 
would
28,30,31
By omitting this study, changes in AHI and minimal SpO2 were 
and low agreement
Moreover, DISE was not associated with better outcomes regarding 
was not associated with a higher success rate after soft tissue surgery 
resulting in contrasted surgical outcomes. Contrariwise, some authors 
only will be treated, neglecting potential secondary obstruction sites 
reaching and surgical outcomes. However, assessment of obstructive sites during DISE is partly subjective and may be sub-
ject to misclassification bias, resulting in discrepancies between differ-
ent 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, mis-
classification of the site or type of collapse and neglect of secondary 
observation 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, inad-
quate 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 retrospec-
tive, 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 under-
treatment depending on the obstructive sites identified and sur-
gregions 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 sur-
gical contra-indication, such as complete concentric collapse in hypop-
glossal stimulation.32 It can also be interpreted that, considering that 
there has been no consensus on DISE indication since its introduc-
tion33 and given that DISE does not seem to be associated with better 
surgical outcomes, DISE might be optional as a first-line setting before 
surgery should be performed based on DISE findings.

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 SpO2 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 multile-
vell surgery addressing the two main sites of obstruction (i.e., the 
velum and the tongue).25

Second, some results are mainly driven by the study by Pang 
et al.10 By omitting this study, changes in AHI and minimal SpO2 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 sub-
ject to misclassification bias, resulting in discrepancies between differ-
ent observers. Indeed, extremely varying interrater reliability has been 
reported but it is generally low to moderate;26–28 and 
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has been reported in non-experienced practitioners.29 Therefore, mis-
classification of the site or type of collapse and neglect of secondary 
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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 mini-
mal SpO2 changes, only omitting the study by Pang et al.10 would have 
changed the results in favour of DISE. These results are pre-
sent in Figure S2.

4 | DISCUSSION

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 (I² 0%, p = 0.49).

4.5 | Influence analyses

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 SpO2 (p = 0.05). Test 
was not performed for the analysis of change in ESS given the small number of studies (N = 2).

3.4 | Risk of publication bias

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impacted pooled OR and 95% CI for success rate. For AHI and mini-
mal SpO2 changes, only omitting the study by Pang et al.10 would have 
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3.4.4 | Epworth sleepiness score

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tion33 and given that DISE does not seem to be associated with better 
surgical outcomes, DISE might be optional as a first-line setting before 
surgery should be performed based on DISE findings.
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), 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 \( \text{SpO}_2 < 90\% \), which seem to be strongly associated with incident cardiovascular disease and mortality. 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. 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.

**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 in the Supporting Information section at the end of this article.

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