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ORIGINAL ARTICLE

Temperature controlled radiofrequency ablation at different sites for treatment of obstructive sleep apnea syndrome: a systematic review and meta-analysis

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Abstract
Background This study seeks to determine the efficacy of temperature controlled radiofrequency tissue ablation (TCRFTA) to alleviate symptoms of obstructive sleep apnea (OSA) and reduce polysomnographic measures of OSA in the first year post-treatment.
Methods Systematic review and meta-analysis. Two independent searches of MEDLINE, EMBASE bibliographic databases, and Evidence Based Medicine Reviews to identify publications relevant to OSA and TCRFTA. Effectiveness of TCRFTA was measured separately for application of TCRFTA at the base of tongue and soft palate, and for multilevel intervention using the respiratory disturbance index (RDI), lowest oxygen saturation (LSAT), Epworth sleepiness scale (ESS), and bed partner's rating of snoring using a visual analogue scale (VAS snoring). The most recent search was conducted in April 2013. Statistical analysis was performed using Review Manager Version 5.2 using a relative measure of effect, i.e., ratio of means (RoM).
Results Our initial search resulted in 29 eligible studies, and subsequently, 20 studies were included in the meta-analysis. Substantial and consistent improvement in PSG and subjective outcomes were observed post-TCRFTA in the base of tongue (BOT) and multilevel surgery groups only. Application of TCRFTA at the BOT was associated with a significant reduction in RDI (RoM 0.60, CI 0.47–0.76), ESS (RoM 0.59, CI 0.51–0.67), and VAS snoring (RoM 0.48, CI 0.37–0.62) and increase in lowest oxygen saturation (RoM 1.05, CI 1.01–1.10). Similarly, a significant reduction in RDI (RoM 0.61, CI 0.47–0.80) and ESS (RoM 0.79, CI −0.71 to 0.88) was observed after multilevel TCRFTA, but substantial heterogeneity between these studies was observed.
Conclusion TCRFTA is clinically effective in reducing RDI levels and symptoms of sleepiness in patients with OSA syndrome when directed at the base of tongue or as a multilevel procedure.

Keywords Sleep apnea syndrome · Sleep apnea · Obstructive · Catheter ablation · Electrocoagulation · Diathermy · Surgical procedures

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Introduction

Obstructive sleep apnea (OSA) is very common in middle aged adults. Using a polysomnography (PSG) derived definition, defined as an apnea hypopnea index (AHI) of >5, it occurs in 20–30 % of males and 10–15 % of females in North America [1]. OSA patients are at increased risk of a number of adverse clinical outcomes. They experience attention deficits, which translates into a two to threefold higher rate of motor vehicular accidents in those with severe disease [2]. There is an independent association between OSA, insulin resistance and type 2 diabetes [3]. Patients with sleep apnea have a higher incidence of hypertension, coronary artery disease and stroke compared to matched subjects without sleep apnea. Patients with moderate to severe untreated OSA have a two to three fold increased risk of all-cause mortality compared to patients without OSA independent of other risk factors, such as obesity and hypertension [4–6].

Continuous positive airway pressure (CPAP) is the main stay of treatment for OSA. In a meta-analysis of 22

randomized trials, CPAP was effective in reducing sleepiness and improving quality of life measures in patients with moderate to severe OSA [7]. Although lacking validation from a randomized trial, multiple observational studies have reported an association between CPAP use and decreased cardiovascular disease and mortality [8–10]. Unfortunately, CPAP is a cumbersome treatment, and many patients are unable to use it. Approximately 20 to 40 % of patients with OSA are unable to use CPAP at all. Of the remainder many do not use CPAP optimally [11–16]. Thus, there is a clear need for alternative therapies in those that are CPAP intolerant. Surgical options are potentially very attractive since continued nightly usage is not required. However, many surgical options have high failure rates and their long-term efficacy has been poorly characterized.

Temperature controlled radiofrequency tissue ablation (TCRFTA) utilizes a probe to deliver temperature controlled energy to the upper airway tissue while sparing adjacent tissues. It results in less pain than more conventional methods thus potentially speeding patient recovery from the procedure. TCRFTA can be applied at the level of the soft palate, base of tongue or both levels depending on the predominant site of obstruction. It can be performed in an office setting, can be repeated as needed, and is associated with less morbidity than an operative procedure.

Comprehensive studies evaluating TCRFTA are lacking. A meta-analysis was published in 2008 evaluating this procedure. Sixteen studies were included in this analysis, of which 3 were randomized and 13 were non-randomized. The most recent paper included in this analysis was published in 2006. In the prior study, studies that involved TCRFTA at the level of the soft palate, base of tongue, or multilevel were mixed together. Their analysis did show an overall reduction in Epworth Sleepiness Scores (ESS) and Respiratory Disturbance Index (RDI) suggesting TCRFTA might be a useful treatment option in patients with sleep apnea. Since the time of the last meta-analysis, additional studies [17, 18] have been published, which allow a site specific analysis. The aim of our systematic review is to provide a more precise estimate of the effectiveness of TCRFTA performed at the level of the soft palate, base of tongue or multilevel for the treatment of sleep apnea.

Methods

Eligibility criteria

We included observational and randomized controlled trials that satisfied the following inclusion criteria: (1) subjects with OSA confirmed by clinical symptoms and a PSG demonstrated RDI≥5; (2) treatment with TCRFTA of the soft palate, base of the tongue or both as a stand-alone procedure; and (3) an English version of the study was available. We excluded citations where: (1) TCRFTA was used with other surgical interventions such as uvulopalatopharyngoplasty and (2) TCRFTA was used for treatment of socially disruptive snoring or upper airway resistance syndrome. If an article reported data for subjects with OSA and socially disruptive snoring and/or upper airway resistance syndrome separately, only the data for subjects with OSA was abstracted.

Search strategy

A comprehensive computer-based search of the published medical literature was performed using MEDLINE (1950 onwards access via Ovid), PubMed, EMBASE (all years access via Ovid), and Evidence Based Medicine Reviews. We used search terms as outlined in Appendix 1.

Selection process

Article titles and abstracts were reviewed by two reviewers (RYB and VRM) to determine article eligibility. If an article was thought to be potentially eligible by either reviewer the full-text article was reviewed. The reference lists of relevant review citations and references of all included citations were checked for additional potentially eligible studies. Disagreements between reviewers were resolved either by discussion or by a third reviewer (MJM).

Data abstraction

One reviewer abstracted data from each eligible study using a self-developed standardized form. A second reviewer verified data abstraction, and conflicts, if any, were resolved mutually or by the third reviewer. We collected basic patient population demographic data as well as information about the surgical intervention such as site, number of session, etc. Outcomes were divided into:

- Objective outcomes: RDI and lowest oxygen saturation (LSAT, %)
- Subjective outcomes: included bed partner's visual analogue scale evaluation of snoring (VAS, 0–10) and ESS

Data analysis

Statistical analysis was performed using RevMan Version 5.2 (Review Manager, Cochrane Collaboration 2012). We used a relative measure of effect i.e., ratio of means (RoM) by calculating the ratio of final mean value post-intervention to the mean value prior to intervention, such that ratio of means <1 favors reduction in outcome. Standard error was calculated as described previously [19], and RoM across studies and its

Table 1 Methodological quality

Outcomes	No. of participants (studies) follow up	Quality of the evidence (GRADE)
Radiofrequency ablation at base of tongue for obstructive sleep apnea		
Respiratory distress index	137	⊕⊖⊖⊖
Polysomnography[1]	(7 studies[2])	Very low[3]
	3–11 months	due to risk of bias
Lowest saturation of oxygen	103	⊕⊖⊖⊖
Polysomnography	(4 studies[2])	Very low[3]
	3–11 months	due to risk of bias
Epworth sleep scale	81	⊕⊖⊖⊖
ESS questionnaire	(6 studies[2])	Very low[3]
		due to risk of bias
Visual analogue scale snoring	46	⊕⊖⊖⊖
Questionnaire	(3 studies[2])	Very low[3] due to risk of bias
	3–4 months	
Radiofrequency ablation multilevel for obstructive sleep apnea		
Respiratory distress index: short-term follow up	243	⊕⊖⊖⊖
Polysomnography	(8 studies[2])	Very low[3,4]
	2–4 months	due to risk of bias, inconsistency
Epworth sleep scale	208	⊕⊖⊖⊖
ESS questionnaire	(7 studies[2])	Very low[3]
		due to risk of bias
Visual analogue scale snoring	134	⊕⊖⊖⊖
Questionnaire	(4 studies[2])	Very low[3,4]
		due to risk of bias, inconsistency
Lowest saturation of oxygen: short term follow up	146	⊕⊖⊖⊖
Polysomnography	(4 studies[2])	Very low[3]
	12–16 months	due to risk of bias

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality: We are very uncertain about the estimate

CI confidence interval

[1] Polysomnography

[2] Case series

[3] Lack of an independent control group

[4] Heterogeneity: I square=93 %

associated confidence interval (CI) were pooled using standard equations for inverse variance weighting using a random effects model [20]. Heterogeneity was expressed by I^2, with I^2 values of 25, 50, and 75 % interpreted to indicate low, moderate, and high heterogeneity, respectively [21]. Each surgical site, i.e., base of tongue, soft palate, and multi-level intervention, was analyzed separately. Since only a small number of studies were analyzed in each group, we considered a funnel plot unreliable in the determination of presence or absence of publication bias [22]. The overall quality of evidence was graded using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [23] (Table 1).

Results

The search process is outlined in Fig. 1. Twenty-nine studies described temperature controlled radiofrequency ablation [24–52] as a stand-alone procedure. Three studies were excluded since only the abstracts were available in the English language and there was not enough information available in the abstract to obtain the relevant outcomes [35, 37, 41]. Attempts to contact the first authors for additional information were unsuccessful. Six studies were excluded from the meta-analysis but not the systematic review because patients with OSA could not be extracted from the group data that included snorers (one study [48]), the mean data was not provided (one study [25]), data was not presented in a way to extract relevant data (one study [24]), and three studies contained duplicate patients, the centers provided their further experience with this technique at a later time [43, 45, 50]. The study from these centers that contained the most extractable data on the most patients was chosen for inclusion. In total, 21 of the 26 studies had full in-laboratory polysomnography at baseline and at follow up [24, 26, 28, 29, 31–34, 36, 38–40, 42, 43, 45–47, 49, 51, 52, 50]. Among the other five studies, three had home or unattended polysomnography data ([25, 30, 44], one had

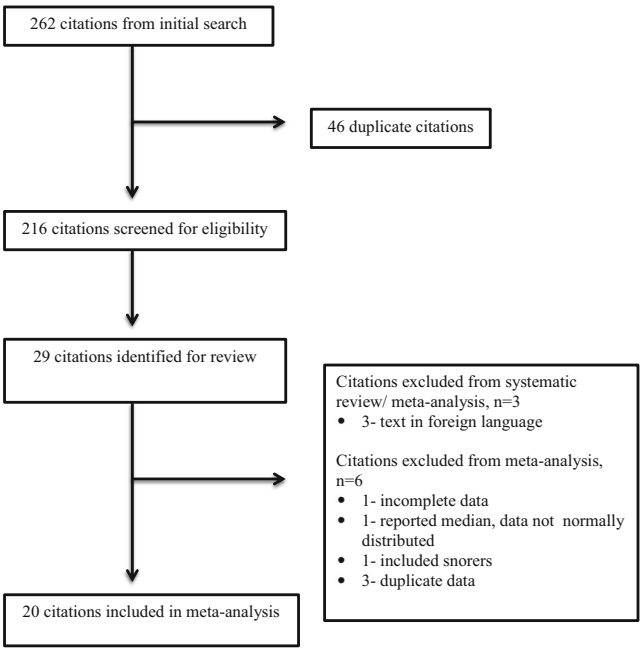

Fig. 1 Search process

level I-III polysomnography based on the clinical probability of severity [27] and one had full polysomnography only at baseline but not at follow up [48].

Based on the site of application of TCRFTA, studies were divided into three groups- base of tongue (BoT), soft palate (SP) and multi-level approach. Tables 2, 3, and 4 contain the methodological qualities and results reported by the 20 studies included in our meta-analysis, and 6 studies (bolded text in table) included in our systematic review but excluded from the meta-analysis as outlined above. Studies were generally of low methodological quality (Table 1).

TCRFTA: base of tongue

Our literature review included three non-randomized, parallel group comparative trials comparing application of TCRFTA at the BoT with either CPAP [51], submucosal minimally invasive lingual excision (SMILE) [34] technique or lingual suspension [32], and seven prospective case series [39, 45, 36, 46, 40, 26, 31].

Respiratory disturbance index (RDI)

The overall mean RDI showed a significant 40 % reduction after treatment (Fig. 2; RoM=0.60, 95 % CI 0.47–0.76, $p<0.0001$, $I^2=51$ %). Five of the seven studies found significant reductions in RDI with TCRFTA at the BoT [39, 51, 40, 26, 32], whereas the remaining two studies [46, 31] showed a non-significant reduction after TCRFTA treatment. Heterogeneity was moderate.

Lowest oxygen saturation (LSAT %)

Short-term (<12 months) post-TCRFTA LSAT improved significantly (RoM=1.05, 95 % CI 1.01–1.10, $p=0.02$, $I^2=37$ %; Fig. 3). Three studies showed a significant improvement, whereas one study showed a non-significant increase with TCRFTA [51]. Heterogeneity was low to moderate.

Epworth Sleepiness Score (ESS) and bed partner's snoring Visual Analogue Scale (VAS)

Short-term (<12 months) reduction in the mean ESS (RoM=0.59, 95 % CI 0.51–0.67, $p<0.00001$, $I^2=0$) and VAS snoring (RoM=0.48, 95 % CI 0.37–0.62, $p<0.00001$, $I^2=0$) was significant (Figs. 4 and 5, respectively). Heterogeneity was low.

Other short-term outcomes

Other reported short-term effects were VAS speech, VAS swallowing, and generic quality-of-life questionnaire (SF-36). Only three studies [39, 46, 40] reported VAS speech and swallowing and statistical analysis showed no significant improvement (VAS speech—RoM 0.92, 95 % CI 0.56–1.49, $p=0.72$, $I^2=94$ %; VAS swallowing—RoM 0.68, 95 % CI 0.31–1.47), $p=0.33$, $I^2=61$ %) post-TCRFTA with significant heterogeneity between studies. Two studies [39, 51] reported the SF-36 health survey, with a homogenous improvement in four of the eight reported domains; role physical—RoM 1.16, 95 % CI 1.02–1.32, $p=0.02$, $I^2=0$; bodily pain—RoM 1.14, 95 % CI 1.06–1.24, $p=0.001$, $I^2=0$; vitality—RoM 1.24, 95 % CI 1.07–1.44, $p=0.004$, $I^2=0$; and social functioning—RoM 1.11, 95 % CI 1.02–1.20, $p=0.01$, $I^2=0$.

Long-term outcomes

Long-term (>12 months) follow up of RDI and ESS was reported by two studies [36, 32]. The RDI showed a significant 36 % reduction (RoM 0.65, 95 % CI 0.53–0.80, $p<0.00001$, $I^2=0$), whereas improvement in ESS was not maintained after 2 years (RoM 0.62, 95 % CI 0.33–1.16, $p=0.13$, $I^2=83$ %). When compared to short-term (<12 months) results, both RDI and ESS demonstrated a trend towards worsening at long-term follow up (>12 months). One study reported a significant improvement in the change scores between post-treatment and long-term follow up for VAS snoring ($p=0.01$), VAS speech ($p=0.02$), VAS swallowing ($p=0.09$), and two of the eight SF-36 domains (vitality, $p=0.05$; social functioning, $p=0.03$); and also the mental component score, $p=0.03$ [36].

Table 2 TCRFTA—base of tongue

Study	Population/type of surgery	Outcomes	Methodological features	Results
Powell et al. [37] Study design: prospective, case series, and pilot study	Participant characteristics: 18 subjects, M/F 17/1, age 44.9 (SD 8.68) year Site of obstruction: base of tongue Prior surgery: palatopharyngoplasty and others Mean no. of sessions and sites per treatment[1]: 5.5 (range 2–9), 2 treatments per session Bipolar/unipolar: N/A Mean Joules[1]: 8,490 (SD 2,687)	Measurement tools: level 1 PSG Subjective outcomes: ESS, Quality of Life using SF-36 Mean follow-up period, 44.3 (11.9; range, 21.1–68.3)weeks	Selection bias: small sample size Information bias: objective outcome measurement- yes, standardized objective outcome evaluation tools- yes Confounding bias: yes Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: severity of OSA and prior surgery Incomplete data: none Withdrawals/loss to follow up: none	PSG: mean RDI (pre 39.6 and post 17.8; p=0.003), AI (pre 22.1 and post 4.1; p=0.023), and LSAT (pre 81.9 % and post 88.3 %; p=0.030) improved significantly post-surgery. Subjective outcomes: ESS scores improved significantly with surgery (p=0.0001). Mean change scores for quality of life (SF-36) were not significant. Complications: 1—linear superficial ulcer, 1—pain on swallowing, 1—tongue infection 3 weeks after 2nd treatment Overall complication rate: 16.6 %
Stuck et al. [43] Study design: prospective, case series	Participant characteristics: 20 subjects, M/F 16/4, age 49.3 (SD 8.46)years Site of obstruction: base of tongue Prior surgery: 5/20-velopharyngeal surgery (tonsillectomy combined with a modified uvulaflap) Mean no of sessions, and sites per treatment: 2 and 4 Bipolar/unipolar: N/A Mean Joules: 2,800[2]	Measurement tools: level 1 PSG Subjective outcomes: ESS, quality of lifeusing SF-36 health survey, VAS for pain, snoring, speech, taste, swallowing, and pharyngeal irritation Mean follow-up period: not reported	Selection bias: small sample size Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: yes Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: BMI, preoperative antibiotic use, and prior surgery Incomplete data: none Withdrawals/loss to follow up: none	PSG: 13 patients (65 %) showed an improvement in OSAS (RDI reduction greater than 50 %, with postoperative RDI less than 20/hour). Five patients (25 %) remained unchanged and 2 patients (10 %) showed deterioration. Mean pre RDI was 28. Mean post-RDI: N/A Subjective outcomes: ESS scores improved more than 20 % in 12 patients (60 %) and remained unchanged in 5 patients (25 %). VAS for pain, snoring, speech, taste, swallowing, and pharyngeal irritation did not change at 4 weeks post 2nd TCRFTA. Complications: tongue swelling—mild 25 and moderate 15, hospital admissions due to severe tongue swelling with dysphagia—4, ulceration of tongue base mucosa—2, and tongue base infection requiring tracheotomy—1. Overall complication rate, 18 %; 2.5 % severe complications Post-treatment complication rate was 5 % with no severe complications in patients who received pre- and post-treatment antibiotics.
Woodson et al. [49] Study design: prospective, non-randomized, parallel group trial	Participant characteristics: TCRFTA group—73 subjects, M/F (%) 92.8/7.2, age 47.13 (SD 9.5)years Site of obstruction: base of tongue Prior surgery: UPPP, tonsillectomy, turbinate reduction, septoplasty, LAUP tongue suspension suture, hyoid suspension, palatoplasty, genioglossus advancement, tracheotomy, and midline glossectomy	Measurement tools: level 1 PSG Subjective outcomes: ESS, quality of life using SF-36, and FOSQ Mean follow-up period, 11 (range 6–12)months	Selection bias: loss to follow up and incomplete data Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: yes Matching: no Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: gender, prior surgery, and baseline SF 36 score	PSG: mean AHI (pre 40.5 and post 32.8; p<0.01) and AI (pre 16.3 and post 11.7; p<0.04) improved significantly post-surgery. LSAT increased post-TCRFTA but was not statistically significant. 12/73 (25 %) patients showed worsening of AHI post-TCRFTA. Subjective outcomes: ESS, FOSQ, VAS snoring, VAS daytime sleepiness, and SF-36 showed significant improvement post-surgery. No significant changes in

Table 2 (continued)

Study	Population/type of surgery	Outcomes	Methodological features	Results
	Mean no of sessions and sites per session: 5.4 (SD 1.8) and 3.1 (SD 0.90) Bipolar/unipolar: N/A Mean Joules: 13,394 (SD 5,459): 2,720 (960)J per session per pt		Incomplete data: TCRFTA—56/73 had both pre- and postoperative PSG, 4/73 initial split night PSG were excluded, 2/73 did not have postoperative PSG, and 1/73 had UPPP during study period. 69/73 provided subjective data. Withdrawals/loss to follow up: TCRFTA—10/73	speech, swallowing, taste, or throat irritation were noted. Complications: tongue abscess—1, infection/cellulitis—7, edema/ecchymosis—3, thrush—1, vasovagal reaction—1, and blindness—1 (TIA related) Overall complication rate, 4.8 %
Li et al. [34] Study design: prospective, case series	Participant characteristics: 18 subjects, M/F 17/1, and age 44.9 (SD 8.7)years Site of obstruction: base of tongue Prior surgery: palatopharyngoplasty and others Mean no of sessions, and sites per treatment[1]: 5.5 (range 2–9); 2 treatments per session Bipolar/unipolar: N/A Mean Joules[1]: 8,490 (SD 2,687)	Measurement tools: level 1 PSG Subjective outcomes: ESS, VAS snoring, speech and swallowing, and SF 36 Mean follow=up period, 28 (SD 4)months	Selection bias: small sample size, loss to follow up Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: yes Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: severity of OSA, prior surgery, and BMI Incomplete data: no Withdrawals/loss to follow up: 2/18	PSG: Persistent improvement in mean AI (pre 22.1, post 4.1, and follow up 5.4) was observed at extended follow up. HI, RDI (pre 39.5, post 17.8, and follow up 28.7), and LSAT showed a trend of worsening. Subjective outcomes: long-term SF-36 and ESS scores demonstrated non-significant trend to improvement compared with baseline, and no differences were found compared with early post-treatment results. VAS measurement for snoring, speech, and swallowing did improve in the immediate post treatment period but this benefit was lost over time. Complications: not reported Overall complication rate: not reported
Stuck et al. [44] Study design: prospective, case series	Participant characteristics: 20 subjects, M/F 16/4, and age 49.3 (SD 8.46)years Site of obstruction: base of tongue Prior surgery: 5/20—velopharyngeal surgery (tonsillectomy with modified uvulopalatal flap) Mean no of sessions and sites per session: 3.4 and 4 Bipolar/unipolar: N/A Mean Joules: 2,800 (SD 700) per session	Measurement tools: level 1 PSG Subjective outcomes: ESS, quality of life using SF-36 health survey, VAS for pain, snoring, speech, taste, swallowing, and pharyngeal irritation Mean follow-up period, 12 weeks after last session	Selection bias: small sample size, loss to follow up Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: N/A Blinding of outcome adjudicator: yes medical assistant involved in PSG blinded to pre- or postoperative measurements Adjustment in analysis: yes Confounding variables: prior surgery Incomplete data: none Withdrawals/loss to follow up: 2/20, 1st—refused to come for follow-up visits and 2nd—declined further treatment due to serious adverse events	PSG: Mean RDI (pre 32.1 and post 24.9) and LSAT (pre 92.3 and post 93.1) improvement post-TCRFTA was not statistically significant. 2/18 (11 %) showed deterioration of SDB; RDI remained unchanged in 6/18 (33 %). Subjective outcomes: significant reduction in ESS (p=0.0004) and VAS snoring (p=0.0001) was observed post-TCRFTA. No relevant changes in VAS speech, taste, swallowing, and pharyngeal irritation were observed. Complications: mild (n=46 treatments) to moderate (n=20 treatments) tongue swelling 1 day after surgery, ulceration of tongue (n=2 treatments), hospitalization due to severe tongue swelling (n=4, 3 patients), and tongue base infection (1 patient) Overall complication rate: 10 %; 1 (1.5 %) severe complication
Riley et al. [38] Study design: prospective and case series	Participant characteristics: 20 subjects, M/F 15/4 (excluded 1 patient who refused follow up polysomnography), and age 49.6 (SD 10.7)years Site of obstruction: base of tongue	Measurement tools: level 1 PSG Subjective outcomes: ESS, VAS swallowing, speech, and sleepiness Mean follow-up period, 3 months	Selection bias: small sample size, loss to follow up Information bias: objective outcome measurement- yes, standardized objective outcome evaluation tools- yes	PSG: significant improvement in mean AHI (pre 35.1 and post 15.1; p<0.001) and LSAT (pre 82 % and post 86.3 %; p<0.001) was observed.

Table 2 (continued)

Study	Population/type of surgery	Outcomes	Methodological features	Results
	Prior surgery: UPPP (2), phase 1—UPPP+ GA (8); Hyoid—phase 1 (1), phase 2—maxillary+mandibular osteotomy (3) and GA (1) Mean no of sessions, and sites per session: 4.6 (0.6), average 3 Bipolar/unipolar: N/A Mean Joules: 7,915 (1,152)–5,636 (1,042): BOT, 2,284 (589): ventral surface of tongue 1,741 (224)J per treatment		Confounding bias: yes Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: yes Confounding variables: prior surgery Incomplete data: 1/20 refused follow-up PSG Withdrawals/loss to follow up: none	Subjective outcomes: Significant improvement in ESS was observed ($p<0.001$). VAS speech and swallow did not change post-TCRFTA (p=NS). Complications: 1—transient tongue neuralgia lasting 2 m Overall complication rate: 1/20 (5 %)
Blumen et al. [24] Study design: prospective, case series	Participant characteristics: 11 subjects, M/F: N/A, and age 57.9 (SD 8.9)years Site of obstruction: 5/10—BOT only obstruction, 4/10—BOT+narrow retropharyngeal airway, and 1/10—BOT+long flaccid epiglottis Prior surgery: 6/10—UPPP, 2/10—septoplasty, and 1/10—maxillomandibular osteotomy Mean no of sessions and sites per session: 3 and 6.1 (2.0) Bipolar/unipolar: N/A Mean Joules: 34,292 (12,758)–14,288 (3251) per session	Measurement tools: level 1 PSG Subjective outcomes: ESS, VAS snoring, discomfort, and pain Mean follow-up period, 4–6 7months after last session	Selection bias: small sample size, incomplete data, and loss to follow up Information bias: objective outcome measurement—yes and standardized objective outcome evaluation tools—yes Confounding bias: yes Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: prior surgery and site of obstruction Incomplete data: 2/10, incomplete treatment (1st—refused 2nd treatment; 2nd—refused 3rd treatment) Withdrawals/loss to follow up: 1/11	PSG: mean RDI (pre 52.0 and post 33.6; p=0.016), AI (pre 40.8 and post 23.2; p=0.005), and LSAT (pre 64.2 and post 75.8; p=0.003) showed significant improvement post-TCRFTA. Mean HI did not change significantly. Subjective outcomes: Significant reduction in mean subjective snoring volume, VAS (p=0.017), and ESS (p=0.011) was observed. Complications: 1/10—severe pain, 1/10—hemi-lingual hypesthesia which resolved in 3 m, and 1/10—mild tongue swelling Overall complication rate, 3/10 (30 %)
Den Herder et al. [29] Study design: prospective, case series	Participant characteristics: Solitary TCRFTA/TCRFTA+additional surgery[2]: 83 subjects, M/F 72/11 Solitary TCRFTA at BOT: 22 subjects, M% 82, age 47.4 (SD 9.4) Snoring: 9 subjects, M% 66, age 45.4 (SD 9.7) Mild OSA: 8 subjects, M% 100, age 48.4 (SD 7.0) Moderate OSA: 4 subjects, M% 87.5, age 45.5 (SD 9.0) Severe OSA: 1 subject, M% 100, age 56 Site of obstruction: base of tongue Prior surgery: UPPP- 7/22, TCRFTA soft palate-1/22 (3×), hyoithyroidpexia-1/22 Mean no of sessions, and sites per session: 1.5 (range 1–3), 6 Bipolar/unipolar: bipolar Mean Joules: 504 per session	Measurement tools: level 1 polysomnogram Subjective outcomes: ESS, VAS snoring, hypersomnolence, pain, globus (foreign body sensation), and swallowing Mean follow-up period, 117.8 (61.6)days for AHI and 360 (132)days for ESS	Selection bias: small sample size, incomplete data, loss to follow up Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes combined patients with snoring without sleep apnea Confounding bias: yes Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: prior surgery Incomplete data: 2 subjects with TCRFTA of SP and hyoidthyroidpexia excluded; 10/22 underwent postoperative polysomnogram Withdrawals/ loss to follow up: 5 subjects refused 2nd session; 2 lost with no follow up	PSG: Changes in AHI were not statistically significant but showed a significant positive trend for the moderate and severe OSA group. Mean AHI for mild OSAS: pre 9.7 vs post 9.8; moderate OSAS: pre 17.6 vs post 9.7; and severe OSAS 34 vs 18.5. Subjective outcomes: ESS>7 was observed in 6 patients, 4/6 showed reduction of <7, 1/6 showed no change, and 1/6 showed an increase. Change in ESS was not statistically significant. Subjective complaints of snoring, hyper somnolence, and globus, calculated by VAS, significantly improved (P=0.0003, P=0.065, and P=0.03, respectively) after TCRFTA. No deterioration in swallowing or speech was observed. Complications: NA for TCRFTA only group Overall complication rate: NA for TCRFTA
Friedman et al. [32] Study design: non-randomized, retrospective, parallel group trial	Participant characteristics: 96 subjects TCRFTA: 48 subjects, M/F 39/9, age 46.1 (SD 11.7)years Site of obstruction: base of tongue Prior surgery: nasal procedures (septoplasty, nasal valve repair, and inferior turbinate reduction), soft palate pillar implants, and UPPP	Measurement tools: level 1 polysomnogram Subjective outcomes: ESS and VAS snoring Mean follow-up period, 6.4 (range, 3–18)months	Selection bias: no Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: yes Blinding of outcome adjudicator: no	PSG: Postoperative PSG showed significant improvement in mean AHI (pre 38.9 and post N/A), AI (pre7.5 and post N/A), and LSAT (pre 85.4 and post N/A). Subjective outcomes: ESS and VAS snoring improved post-surgery.

Table 2 (continued)

Study	Population/type of surgery	Outcomes	Methodological features	Results
	Mean no of sessions and sites per session: 1 and 10 Bipolar/unipolar: N/A Mean Joules: 3,000		Adjustment in analysis: yes Confounding variables: none Incomplete data: excluded patients with incomplete data Withdrawals/loss to follow up: retrospective study	Complications: TCRFTA: temporary, unilateral, and hypoglossal nerve injury 1
Fibbi et al., [30] Study design: non-randomized,parallel group trial	Participant characteristics: 26 subjects TCRFTA: 13 subjects, M/F 9/3, and age 50.2 (SD 9.1)years; 1 subject excluded from analysis Prior surgery: none Mean no of sessions and sites per session: 2 and 3 Bipolar/unipolar: bipolar Mean Joules: 4,800–2,400 (800) per session	Measurement tools: level 1 polysomnogram Subjective outcomes: ESS and VAS satisfaction Mean follow-up period: evaluated at 1 week 1, 3, and 6 months, and 2 years	Selection bias: small sample size and incomplete data Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: yes Matching: no Blinding of outcome adjudicator: no Adjustment in analysis: yes Confounding variables: BMI Incomplete data: TCRFTA: 1 had a significant increase in BMI; post TCRFTA patient was excluded. Withdrawals/loss to follow up: none	PSG: significant improvement in mean AHI after 6 months post-TCRFTA (pre 14.8 and 6 months 4.7), but this difference was slightly less significant at 24 months (8.7/hour) Subjective outcomes: Sleepiness using ESS and VAS satisfaction showed a general improvement at 6 months, which was partly retained at 2 years. Complications; TCRFTA—minor, 4—edema, mucosal erosion, and pharyngodynia Overall complication rate: TCRFTA—minor—31 %

Adverse events

Adverse events following TCRFTA were reported by most studies (Tables 2, 3, and 4). Side effects of treatment included ulceration of the tongue base mucosa, odynophagia, pharyngodynia, mild-to-severe tongue edema, ecchymosis, hematoma, transient neuralgia, transient tongue deviation, and hypoglossal nerve injury. Eight cases of infection and two cases of tongue base abscess were reported by studies that did not use perioperative antibiotic prophylaxis [39, 51, 46]. Oral thrush and postoperative vasovagal reaction were relatively rare complications.

TCRFTA: soft palate

Five articles describing outcomes following TCRFTA of the SP were included [28, 27, 48, 24, 25] (Table 3) in the review

Respiratory Disturbance Index (RDI)

After excluding Terris et al. [48], a study that lacked follow up PSG data, the remaining two observational studies [28, 27] were included in the analysis. A non-significant trend towards improvement of short-term mean RDI (RoM 0.67, 95 % CI 0.43–1.03, $p=0.07$, $I^2=83$ %) was observed with significant heterogeneity between the two studies.

Epworth Sleepiness Score (ESS) & bed partner's snoring Visual Analogue Scale (VAS)

One study [24] did not report ESS, all five studies reported VAS scores. ESS did not improve significantly with TCRFTA treatment (RoM 0.85, 95 % CI 0.63–1.15, $p=0.29$, $I^2=0$ %), However, reduction in mean VAS snoring was significant (RoM 0.39, 95 % CI 0.30–0.50, $p<0.00001$, $I^2=0$ %).

TCRFTA: multilevel

Eleven articles were identified by literature search and reviewed in detail (Table 4). Nine of the 11 studies met inclusion criteria for the meta-analysis [33, 52, 42, 47, 44, 29, 38, 49, 30]. Only one study was a randomized controlled prospective trial [52], two were non-randomized comparative parallel group trials [42, 38], and the remaining six were either prospective [33, 47, 44, 29, 49] or retrospective [30] case series. Although most studies restricted application of radiofrequency to the BoT and SP only, three studies [33, 29, 30] included additional sites such as nasal turbinate and tonsils.

Respiratory Disturbance Index (RDI)

Short-term improvement in RDI was calculated using one randomized, and seven observational studies (Fig. 6). The

Table 3 TCRFTA—soft palate

Study	Population/type of surgery	Outcomes	Methodological features	Results
Brown et al. [26] Study design: non-randomized, prospective case series	Participant characteristics: 12 subjects, M/F(%) 100, and age 45 (26–53)years Site of obstruction: soft palate and base of tongue Prior surgery: tonsillectomy Mean no. of sessions and sites per session: 3 and 3 Bipolar/unipolar: N/A Mean Joules: 1,200 per session	Measurement tools: level 1 PSG Subjective outcomes: ESS Mean follow-up period: 6 weeks after last treatment	Selection bias: small sample size, incomplete treatment in 1/12 Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: site of obstruction and prior surgery Incomplete data: 1/12 declined 3rd treatment Withdrawals/loss to follow up: none	PSG: Significant improvement in AHI (pre 31.2 and post 25.3) was observed. LSAT (pre 84.4 and post 83.3) did not improve post-treatment. Subjective outcomes: Changes in ESS, snoring scale, and speech and swallowing difficulty were not statistically significant. Complications: mucosal edema, 1—observed overnight, 3—mucosal ulceration Overall complication rate: 3/12 (25 %)
Blumen et al. [25] Study design: non-randomized, prospective case series	Participant characteristics: 78 patients had TCRFTA, 29 patients completed full BOT protocol, and 4 patients had combined TCRFTA procedures. M/F 26/3, age 57.4 (9.2)years Site of obstruction: soft palate Prior surgery: none Mean no of sessions, and sites per session: Multiple protocols used Bipolar/unipolar: N/A Mean Joules: varied based on protocol used	Measurement tools: Level 1, 2, or 3 PSG Subjective outcomes: ESS, bed partner, and snoring volume using a VAS scale Mean follow-up period: clinical—11.0 (4.7)weeks; PSG—8.5 (3.8)months after the last procedure	Selection bias: small sample size and loss to follow up Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: none Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none Incomplete data: 8 incomplete data Withdrawals/loss to follow up: 37 did not return for 2nd treatment	PSG: Significant reduction in mean RDI (pre 19.0 and post 9.8) was observed ($p<0.001$). 25/29 subjects showed improvement, whereas 4/29 showed worsening of RDI post TCRFTA.19/29 subjects were considered cured of OSAS (RDI<10). 4/19 did not show improvement in ESS and had higher micro arousals after ablation. LSAT (pre 85.3 and post 86.4) increased non-significantly post-TCRFTA ($p=0.35$). Subjective outcomes: Mean snoring level and ESS decreased in 28/29 subjects and 18/29 subjects, respectively, post-TCRFTA. Decrease in the mean VAS snoring score was significant ($p<0.0001$) but not ESS ($p=0.15$). Complications: 3/11 subjects in one of the protocols developed soft palate perforation Overall complication rate: 3/29 (10.3 %)
Terris et al. [46] Study design: randomized, prospective clinical trial	Participant characteristics: TCRFTA 12 subjects, sex N/A, and age 52.8 (12.1)years Site of obstruction: soft palate Prior surgery: none Mean no. of sessions and sites per session: 3 or less and 3 per session Bipolar/unipolar: N/A	Measurement tools: preoperative level 1 polysomnogram, Subjective outcomes: ESS, VAS snoring, pain, speech, and swallowing Mean follow-up period, 16 weeks	Selection bias: small sample size, loss to follow up, incomplete data Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: yes Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none	PSG: Postoperative PSG data not available. Mean pre-AHI 5.4 Subjective outcomes: 6/10 (60 %) achieved a satisfactory reduction in the volume of snoring, as reported by the sleep partner (VAS snoring 7.5 (2.1) to 3.1 (2.6), $p=0.0006$). ESS reduction post-TCRFTA was not statistically significant ($p=0.24$).

Table 3 (continued)

Study	Population/type of surgery	Outcomes	Methodological features	Results
	Mean Joules: 1,090 (136)J per session. Energy reduced from 600+300×2 to 1,000 if ulcerations noted		Incomplete data: Postoperative data not available in a home based diagnostic test (SNAP Laboratories): TCRFTA—7/12 Withdrawals/loss to follow up: TCRFTA—2/12	Complications: No differences in speech was noted (p=0.96). Overall complication rate: N/A
Atef et al. [22] Study design: randomized, prospective comparative trial	Participant characteristics: TCRFTA with uvulectomy: 75 subjects, sex, amd age N/A Site of obstruction: soft palate Mean no. of sessions, and sites per session: 1–5 and 4–5 per session Bipolar/unipolar: N/A Mean Joules: N/A	Measurement tools: level 1 polysomnogram Subjective outcomes: VAS Mean follow-up period, 3 (early) and 18 months (late)	Selection bias: incomplete data, exclusion of subjects with incomplete data Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: no Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none Incomplete data: postoperative polysomnogram not performed, TCRFTA 11/75 Withdrawals/loss to follow up: none	PSG: Postoperative RDI decreased significantly in subjects who received 3 or more TCRFTA treatments at 3 (3 p=0.01, 4 p=0.00, and 5 p=0.00) and 18 months (3 p=0.04, 4 p=0.00, and 5 p=0.00). Mean AHI, pre and post procedure, N/A Complications: N/A Overall complication rate: N/A
Back et al. [23] Study design: prospective, randomized, placebo controlled trial	Participant characteristics: 32 subjects, M/F % 100, and age 30–65 years TCRFTA: 17 subjects, M/F (%) 100, and age 30–65 years Placebo: 15 subjects, M/F (%) 100, and age 30–65 years Site of obstruction: velopharyngeal Mean no. of sessions and sites per session: 1 and 5 Bipolar/Unipolar: bipolar Mean Joules: N/A	Measurement tools: level 1 polysomnogram Subjective outcomes: VAS pain, swelling sensation of the SP, difficulty in drinking, breathing, speaking, and opening the mouth, VAS snoring by bed partner, ESS, and SF-36 survey (36 item short-form health survey) Mean follow-up period: median 4 m (range: 4–6 m)	Selection bias: small sample size and incomplete data Information bias: objective outcome measurement- yes, standardized objective outcome evaluation tools- yes Confounding bias: no Matching: yes Blinding of outcome adjudicator: yes Adjustment in analysis: yes Confounding variables: none Incomplete data: TCRFTA—2/17 did not fill SF-36 questionnaires; 1/17 was living without a bed partner. Placebo—1/15 was living without a bed partner Withdrawals/loss to follow up: none	PSG: No statistically significant changes in the mean RDI (pre 11 and post 13), LSAT (pre 82 and post 82 %), and average saturation % (pre 94 % and post 94 %) were observed. Subjective outcomes: Statistically significant difference in VAS scores of swelling sensation persisted after 1 week. None of the patients reported any treatment related symptoms or complications at 4 months. No significant improvement in snoring questionnaires, ESS, and SF36 survey was observed. Complications: not reported Overall complication rate: N/A

Table 4 TCRFTA—multilevel

Study	Population/type of surgery	Outcomes	Methodological features	Results
Woodson et al. [50] Study design: prospective, randomized, placebo controlled trial	Participant characteristics: TCRFTA: 30 subjects, M% 89.7, and age 49.4 (9.2)years Site of obstruction: excluded tonsillar hypertrophy, nasal, or supraglottic obstruction Prior surgery: none Mean no of sessions and sites per session: TCRFTA at BOT—4.5 (0.8) and 2.8 (0.5) lesions per session; soft palate—1.5 (0.7) and 2.7 (0.8) lesions per session. Placebo—2.9 (0.4) and 2.7 (0.5) lesions per session at BOT only. Bipolar/unipolar: N/A Mean Joules: TCRFTA—BOT—9,700 (2,000), SP—1,785 (904), placebo—0. 2,144 (375) per session BOT, 1,129 (330) per session SP 770 (118) per lesion BOT, 624 (74) midline, 309 (29) lat SP. Other data available. Total BOT 9,700 (2,000), 1,785 (904) SP	Measurement tools: level 1 PSG Subjective outcomes: ESS, SF-36, VAS pain, swallowing, and snoring Mean follow-up period: 8 weeks	Selection bias: small sample size, loss to follow up, and incomplete data Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: yes Matching: yes, age different at baseline (p=0.04) Blinding of outcome adjudicator: incomplete, randomization concealed using sealed envelopes, patients single blinded to TCRFTA or placebo, PSG, and questionnaire staff blinded Adjustment in analysis: no Confounding variables: age Incomplete data: TCRFTA—3, CPAP—7, and placebo—3 Withdrawals/loss to follow up: TCRFTA—2 lost to follow up, 1 discontinued after 2 treatments, 2 discontinued after 3 treatments, and 3 discontinued after 4 treatments. One failed inclusion criteria (AHI<5) and 1 withdrew prior to intervention. Placebo—1 lost to follow up, 1 discontinued after 1 treatment, and 1 withdrew prior to intervention	PSG: No statistically significant change from baseline in AHI, AI, and LSAT (pre and post-data N/A) was observed post TCRFTA or placebo compared to baseline. When compared to placebo, TCRFTA showed a significant improvement in AI (mean difference of 4.8 favoring TCRFTA, p=0.02). SF-36 MCS showed a non-significant improvement post-TCRFTA (p=0.08). Complications: TCRFTA, BOT: 3 hematoma, 1 ulceration, and 0 infections; TCRFTA, soft palate: none; Placebo: 3 hematoma, 0 ulceration, and 0 infections Overall complication rate: 3.1 %
Fischer et al. [31] Study design: non-randomized, prospective case series	Participant characteristics: 16 subjects, M/F—13/3, and age 56.0 (11.1)years Site of obstruction: BOT+SP+tonsils Prior surgery: no prior velopharyngeal or lingual surgery Mean no of sessions, and sites per session: 1, SP—5, T—4 per side, and BOT—4 (total 16 sites) Bipolar/unipolar: N/A Mean Joules, 9,750 J. SP 2,750 (5 s), tonsil 2,000 (4 s × 2), and BOT 3,000 (3 s)	Measurement tools: level 1 PSG Subjective outcomes: ESS, VAS speech, swallowing and sore throat, and VAS snoring Mean follow-up period, 20.6 (12.6)weeks postop (range, 12–56 weeks)	Selection bias: small sample size and loss to follow up Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: no Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none Incomplete data: none Withdrawals/loss to follow up: 1/16	PSG: Statistically significant reduction in post-TCRFTA mean RDI was observed (mean pre-RDI of 32.6 vs post-RDI of 22.0, p=0.003). RDI remained unchanged in 5/15 patients and 1/15 patients showed deterioration. Subjective outcomes: Significant reduction in mean ESS was observed post-TCRFTA (p=0.0001). No patient showed deterioration of ESS, 8/15 showed no change. Mean VAS snoring showed a non-significant improvement (p=0.08). Complications: 1—superficial soft palate ulceration; 1 unilateral tonsillar abscess which required an incision and tonsillectomy Overall complication rate: 13.3 %
Steward [40] Study design: non-randomized, retrospective case control study	Participant characteristics: TCRFTA: 22 subjects, M/F (%) 86.4, and age 46.9 (9.9)years Site of obstruction: BOT+ SP+ tonsils (90 %—0 or 1+ tonsil size and 10 % 2+ tonsil size) Prior surgery: CPAP in 6/22, LAUP 1/22, and UPPP 1/22 Mean no of sessions, and sites per session: 4.2 (2–5), 3–4 per session at BOT, 1.8 (1–3), and 3 per session at SP Bipolar/unipolar: N/A Mean Joules: 9,500 at BOT, 2,350 at SP750 per lesion at BOT, 650 midline at base of uvula, and 325 or 350 on either side of midline	Measurement tools: level 1 PSG at baseline Subjective outcomes: ESS Mean follow-up period, 2 months for CPAP group	Selection bias: small sample size, loss to follow up Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: yes Matching: yes Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: untreated tonsillar hypertrophy Incomplete data: TCRFTA—ESS 4/22 and RAI 1/22 Withdrawals/ loss to follow up: TCRFTA 7/22 and CPAP 1/11	PSG: Statistically significant reduction in most PSG indices (AHI mean change of −12.2, p=0.001,; AI mean change of −5.5, p=0.02; HI mean change of −6.9, p=0.03,; RAI mean change of −13.1, p=0.0002) was observed post-TCRFTA. No significant improvement was noted for the LSAT (mean change of 0.1, p=0.96). Subjective outcomes: a statistically significant improvement in ESS (p=0.0001 Complications: No patients experienced airway obstruction, tongue base abscess, or infection.1—SP cellulitis, 3—mucosal ulceration of SP, 3—mucosal ulceration of BOT, and 1—floor of mouth hematoma at BOT; SP—4/41 sessions and BOT—5/93 sessions

Table 4 (continued)

Study	Population/type of surgery	Outcomes	Methodological features	Results
				Overall complication rate: 10 and 5 % for SP and BOT, respectively, per treatment session
Steward et al. [41] Study design: prospective follow up of study arm of a prior randomized controlled trial	Participant characteristics: 29 subjects, M% 89.7, and age 49.4 (9.2)years Site of obstruction: SP+BOT Mean no of sessions and sites per session: Interim: 3.0 (0.2) and 2.9 (0.4) per session at BOT. Final: 1.6 (0.7) and 2.5 (0.7) per session at BOT, and 1.5 (0.7) and 2.7 (0.8) per session at SP Bipolar/unipolar: N/A Mean Joules: Interim—6,689 (844) at BOT. Final—3,047 (1,520)J at BOT and 1,785 (904) at SP. 777 (87) per lesion interim BOT, total energy Final: 755 (163) BOT, 624 (74) midline SP, and 309 (29) lat SP per lesion	Measurement tools: level 1 and 2 PSG at baseline only Subjective outcomes: ESS Mean follow-up period, 1 month post initial 3 BOT treatments at a 4-week interval and 2 months post 2nd treatment of additional 2 BOT/ SP treatments	Selection bias: small sample size, loss to follow up Information bias: objective outcome measurement-yes, standardized objective outcome evaluation tools- yes Confounding bias: no Matching: no Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none Incomplete data: 3/29 Withdrawals/ loss to follow up: 1 excluded before randomization and 3 drop outs	No PSG outcomes Subjective outcomes: Compared to baseline interim follow-up data showed a trend towards improvement in ESS ($p=0.06$). After additional treatment sessions, final outcomes showed a significant improvement in ESS ($p=0.03$) Complications: 3 hematomas and 1 mucosal ulceration Overall complication rate: 3.1 %
Stuck et al. [45] Study design: prospective, clinical trial	Participant characteristics: 20 subjects, M/F 16/4, and age 49.6 (8.72)years Site of obstruction: SP+BOT Prior surgery: none Mean no of sessions, and sites per session: mean 2.7 sessions. Maximum 4, 4 sites per session at BOT, and 3, 3–4 per session at SP Bipolar/unipolar: N/A Mean Joules: 2,800 at the BOT, 1,500 (3 sites)–1,800 (4 sites) per session	Measurement tools: level 1 PSG Subjective outcomes: ESS, SF-36, VAS snoring, speech, taste, swallowing, pharyngeal irritation, pain, and dysphagia Mean follow-up period, 12 weeks	Selection bias: small sample size, loss to follow up, incomplete data Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: none Matching: no Blinding of outcome adjudicator: yes, PSG medical assistant blinded to pre- or postoperative measurements Adjustment in analysis: no Confounding variables: none Incomplete data: VAS snoring measured in 16/18 only, 1/20 did not undergo final PSG Withdrawals/ loss to follow up: 2/20	PSG: Significant reduction in mean RDI was observed (mean pre-RDI of 25.3 vs mean post-RDI of 16.7, $p<0.05$). RDI worsened in 1/18 cases and remained unchanged in 5/18 cases. LSAT did not differ significantly post-TCRFTA ($p>0.05$). Subjective outcomes: Significant reduction in mean ESS ($p<0.05$), VAS snoring ($p<0.05$), and 6/8 aspects of SF-36 ($p<0.05$) were observed. ESS increased in 2/18 cases and remained unchanged in 4/18. VAS snoring improved in 16/18 cases (overall $p<0.05$). Differences in VAS speech, taste, swallowing, and pharyngeal irritation at 12 weeks were not significant. Complications: Postoperative swelling at the BOT on Day 1 was absent ($n=12$ treatments) or mild ($n=37$ treatments), and moderate after 2 treatments. It was absent ($n=6$ treatments), mild ($n=25$ treatments), moderate ($n=17$ treatments), or severe ($n=2$ treatments) for the SP. Overall complication rate: 39/51 (76.5 %) BOT and 44/50 (88 %) SP treatments
Steward et al., 2005 [42] Study design: prospective follow up of study arm of a prior randomized controlled trial, case series	Participant characteristics: 29 subjects, M (%) 79, and age 49 (9)years Site of obstruction: SP+BOT Prior surgery: none Mean no of sessions, and sites per session: 3.3 (1.5)/3 at the BOT, 2.0 (0.6)/1–3 at the SP Bipolar/unipolar: N/A Mean Joules: 6,500 (3,800) at the BOT, 2,200 (800) at the SP. 650 midline, 325 either sides-palate, and 600–1,100 BOT	Measurement tools: level 2 PSG Subjective outcomes: ESS Mean follow-up period: long-term median 23 months (range, 19–31), short-term median 9 weeks (8–11)	Selection bias: small sample size, sampling bias, and incomplete data Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: yes Matching: no Blinding of outcome adjudicator: Adjustment in analysis: Confounding variables: no. of sessions and energy delivered Incomplete data: PSG only in 22/29 Withdrawals/loss to follow up: no	PSG: Significant reduction in AHI (mean change from baseline of 10.4) was observed at long-term follow up ($p=0.01$). Subjective outcomes: Most outcomes improved at a long-term follow up, including ESS ($p<0.001$) Complications: NA
Neruntarat and Chantapant [36]	Participant characteristics: 72 subjects, M/F 69/3, and age 35.8 (10.9)years	Measurement tools: level 1 PSG	Selection bias: loss to follow up	PSG: 48/72 cases showed at least 50 % reduction in AHI and a final AHI≤20 (mean baseline AHI 35.6,

Table 4 (continued)

Study	Population/type of surgery	Outcomes	Methodological features	Results
Study design: prospective, case series	Site of obstruction: SP+BOT Prior surgery: N/A Mean no. of sessions and sites per session: 3.5 (0.7)/3 for SP and 4.8 (0.8)/3 for BOT Bipolar/unipolar: bipolar Mean Joules: 600 J median, 300 J paramedian, and BOT 3 sites of 700 J each per session	Subjective outcomes: ESS, VAS snoring, and pain Mean follow-up period: short term at 3 months and long term at 14.2 (1.8)months, range 12–16 months	Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none Incomplete data: no Withdrawals/loss to follow up: 8/80 withdrawals	short-term AHI 12.5, and long-term AHI 16.8). 40/72 sustained this response. Similarly, mean LSAT improved post-intervention at 3 months and long-term follow up Subjective outcomes: Significant reduction in ESS was observed at 3 months and long-term follow up ($p<0.001$). A significant difference was observed between short and long-term follow up ($p<0.05$). Recurrence of sleepiness was observed in 8/72 cases. VAS snoring improved significantly at 3 months ($p<0.001$) and long term ($p<0.01$). Significant difference was observed between short and long-term results ($p<0.05$). 50 % reduction in VAS snoring was observed in 56/72 cases at 3 months and 50/72 at long term. Complications: palatal ulcer (6/72), lingual ulcer (6/72), dysphagia (6/72), swelling of the floor of the mouth (5/72), and aspiration (5/72) Overall complication rate: 28/72 (38.9 %)
Uloza et al. [47] Study design: prospective, case series	Participant characteristics: 37 subjects, M/F 30/7, and age 41.33 (9.69)years; OSAS, 28 subjects Site of obstruction: not defined Prior surgery: N/A Mean no of sessions and sites per session: 2/9 SP and 8 BOT per session Bipolar/unipolar: N/A Mean Joules: SP at 10 W and BOT at 6 W	Measurement tools: level 1 PSG Subjective outcomes: ESS Mean follow-up period, 2–3 months after 2nd session	Selection bias: small sample size Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none Incomplete data: no Withdrawals/loss to follow up: no	PSG: Mean RDI (pre and post-RDI N/A) showed a trend towards statistical significance after TCRFTA ($p=0.065$). Subjective outcomes: Significant improvement in ESS ($p<0.05$) and VAS snoring ($p<0.001$) Overall complication rate: N/A
Ceylan et al. [27] Study design: prospective, non-randomized, case series Funding: none	TCRFTA: 26 subjects, M/F 23/3, and age 46.3 (3.9) years Site of obstruction: SP+BOT+nasal turbinates Prior surgery: N/A Mean no of sessions, and sites per session: 1/ 3 turbinate sites, 3 SP sites, and 10 BOT sites Bipolar/unipolar: N/A Mean Joules: 350 J/site at 3 sites of the turbinate, 650 J at midline+325 J at 2 lateral SP sites, and 3,000 J at 10 sites over the BOT	Measurement tools: level 1 PSG Subjective outcomes: ESS Mean follow-up period, 12 months	Selection bias: small sample size Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: yes Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none Incomplete data: no Withdrawals/loss to follow up: no	PSG: Significant reduction in mean AHI (mean pre 29.6 vs post 16.1, $p<0.001$) and LSAT (mean pre 86.8 and post 94.6, $p<0.001$) observed post-TCRFTA No significant difference was observed in the treatment success between the TCRFTA and CPAP, 53.8 and 52.4 %, respectively ($p=0.92$). Subjective outcomes: mean ESS improved significantly after TCRFTA ($p=0.003$) Complications: none Overall complication rate: NA
Uloza et al. [48] Study design: prospective, non-randomized case series	29 subjects with OSAS, M/F, and age NA for OSAS patients Site of obstruction: N/A Prior surgery: N/A Mean no of sessions and sites per session: 2/9 SP and 8 BOT per session Bipolar/unipolar: N/A Mean Joules: SP at 10 W and BOT at 6 W	Measurement tools: level 1 PSG Subjective outcomes: ESS and VAS snoring Mean follow-up period, 2–3 months after 2nd session	Selection bias: small sample size Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: none Incomplete data: no	PSG: mean AHI improved significantly (pre 15.75 and post 12.38, $p=0.022$) in OSA group after TCRFTA. Subjective outcomes: Significant improvement in ESS ($p<0.001$) and VAS snoring ($p<0.001$) Overall complication rate: N/A

Table 4 (continued)

Study	Population/type of surgery	Outcomes	Methodological features	Results
De Vito et al. [28] Study design: retrospective, case series	OSAS: 36 subjects, sex, and age N/A Site of obstruction: SP+BOT+IT+GM+PT Prior surgery: nose (septoplasty, turbinoplasty, etc.), uvulopalatoplasty with or without tonsillectomy and anterior-inferior hyoid suspension, as Stanford phase I surgical protocol Mean no of sessions and sites per session: SP—3, genioglossus muscle—3, BOT—6, and inferior turbinate—2 Bipolar/unipolar: bipolar Mean Joules per site: 1,999–2,001 (SP—326, inferior turbinate—270, BOT—328, genioglossus muscle—183, and palatine tonsils—180) and 2002–2009 (SP—175, inferior turbinate—176, and BOT—183)	Measurement tools: level 1 PSG Mean follow-up period: PSG at least 6 months post-TCRFTA	Withdrawals/ loss to follow up: no Selection bias: small sample size Information bias: objective outcome measurement—yes; standardized objective outcome evaluation tools—yes Confounding bias: no Matching: N/A Blinding of outcome adjudicator: no Adjustment in analysis: no Confounding variables: no Incomplete data: no Withdrawals/loss to follow up: no	PSG: At 6 months post-TCRFTA, a significant reduction in mean RDI was observed (mean pre 18.1 to mean post 12.9, $p<0.0001$). No subject had postop AHI less than 5/hour. Complications: light bleeding of the inferior turbinate—20, light scarring of SP—40, and superficial edema of BOT—2 Overall complication rate: NA

overall 41 % reduction in mean RDI was significant (RoM 0.59, 95 % CI 0.45–0.79, $p=0.0003$, $I^2=93$ %), but the results were significantly heterogeneous ($p<0.00001$) between the included studies. Sub-group analysis identified two studies that reported significantly better results as compared to the other included articles [29, 38]. Neruntarat and Chantapant [38] and Ceylan et al. [29] reported a 65 and 46 % reduction in RDI with TCRFTA respectively. The patients in these two studies were somewhat less obese on average than those from the remaining studies and this might be responsible for the different success rates. Indeed, in one of these studies (36), BMI was a univariate predictor of surgical success. We reanalyzed the data excluding these studies. The remaining six studies continued to show a significant reduction in RDI (RoM 0.70, 95 % CI 0.63–0.77, $p<0.00001$, $I^2=0$ %) with a high-level of agreement between the pooled studies (Fig. 7).

Lowest oxygen saturation (LSAT %)

Pre- and post-TCRFTA LSAT were reported by one randomized and three observation studies [52, 42, 29, 38]. There was a non-significant trend towards a short-term increase in LSAT with treatment (RoM 1.03, 95 % CI 1.00–1.06, $p=0.08$, $I^2=$ 73 %), but significant heterogeneity was noted ($p=0.01$) (Fig. 8).

Epworth Sleepiness Score (ESS) & bed partner's snoring Visual Analogue Scale (VAS)

Seven of the included nine studies reported short-term post-treatment ESS, including one randomized prospective placebo controlled trial [52] and six observational studies [33, 42, 47, 29, 38, 49]. Four observational studies reported VAS snoring [33, 47, 38, 49]. Initial analysis showed significant heterogeneity between the results of these trials. After exclusion of the two studies that showed unusually favorable results [29, 38], a significant 22 % reduction in short-term mean ESS (RoM 0.78, 95 % CI 0.69–0.89, $p=0.0001$, $I^2=0$ %) and 46 % reduction in mean VAS snoring (RoM 0.54, 95 % CI 0.41–0.70, $p<0.00001$, $I^2=59$ %) were observed (Fig. 9).

Discussion

Untreated OSA has a number of adverse clinical implications. CPAP is a well-validated first line treatment option for OSA; however, a substantial number of patients are unable to use CPAP. Among surgical options, UPPP is the best studied; however, limited effectiveness, potential complications, and a prolonged recovery [53] make it less attractive.

TCRFTA appears to be a safe alternative that can be used in conjunction with surgery or as a stand-alone procedure. It can be performed safely, potentially as an outpatient procedure

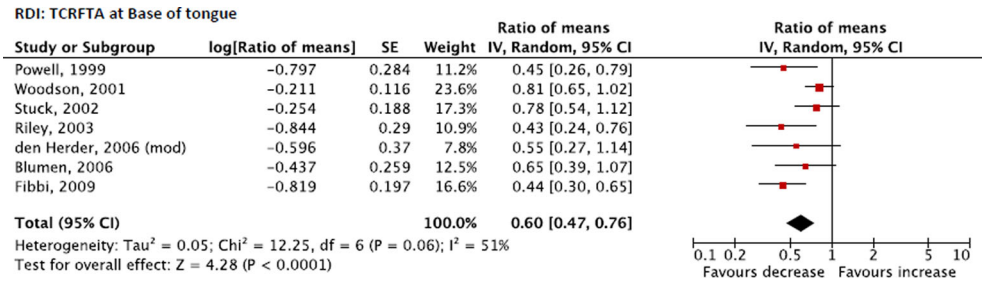

Fig. 2 RDI: TCRFTA at base of tongue

under local anesthesia. The procedure can be repeated in several sessions to achieve the desired result. Radiofrequency ablation can be performed at the base of the tongue, soft palate or as a multi-level procedure, while safely sparing adjacent tissue.

Due to significant heterogeneity between studies, it is hard to draw any strong conclusions on the ideal patient population who will benefit from TCRFTA. However we can state the following:

1. Flexible nasopharynoscopy with Mueller's maneuver (to verify site of obstruction) and cephalometric radiography (to rule out concomitant skeletal abnormalities) are adjunct tests to physical examination that may aid in patients selection. Other tests to be considered included volumetric tongue MRI and drug induced sleep endoscopy (DISE). DISE is emerging as the tool of choice to plan surgical therapy for sleep apnea. A recent study suggested that DISE provided more information on the site of obstruction in the upper airway particularly regarding the hypopharynx than awake screening tools [54]. However, consensus on an accepted scoring and classification system has yet to be achieved [55]. Nevertheless, future trials on TCRFTA will likely use DISE for patient selection. .
2. Most studies evaluated this therapy in patients less than 65 years of age with a BMI<35.
3. TCRFTA has been trialed mostly in mild to moderate OSA. Data is sparse in the severe OSA group.
4. Majority of the studies included patients who had failed other modalities such as CPAP or mandibular advancement devices.
5. Some trials included patients with prior pharyngeal surgery; however, most excluded these patients.

Most trials excluded patients with severe underlying co morbidities, high surgical risk profiles or history of pacemakers.

Complications can occur but appear to be less frequent than in surgical upper airway procedures. Our review primarily aimed at examining the short-term efficacy of TCRFTA performed at different anatomical sites. The primary outcomes variables available for analysis were polysomnography based (RDI and LSAT), a measure of sleepiness and reduction in snoring.

TCRFTA at base of the tongue

We found significant reductions in RDI, LSAT, ESS and snoring. This suggests that this procedure has efficacy at least in the short term. There was considerable heterogeneity between subjects within studies with some subjects not showing any improvement or occasionally even worsening after the procedure. In addition, it would be useful to know how many subjects had a reduction in AHI to less than 15/hour or 10/hour after the procedure, but this information was rarely reported. Subjects whose AHI remains above 15/hour or above 5/hour with residual sleepiness would be considered to require additional therapy. There are now more options for treatment for sleep apnea than there was in the past. Mandibular advancement device efficacy has been well characterized and they have the advantage that if ineffective the patients just needs to stop using them. In contrast, if TCRFTA is ineffective, the patient has gone through a surgical procedure with possible side effects without benefit. Nevertheless, there are patients who would be willing to accept this risk if it meant that they might not have to use a nightly therapy. Our meta-analysis suggests promising short-term results. Longer-term results

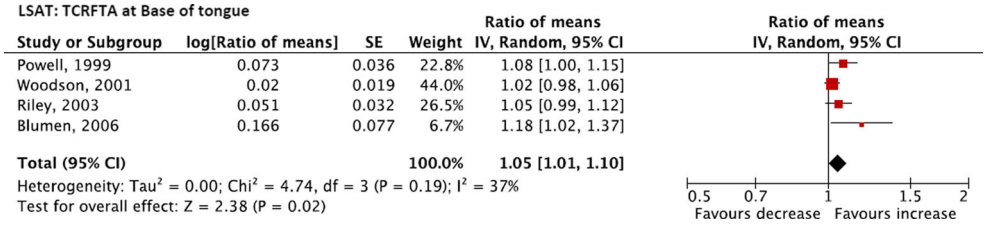

Fig. 3 LSAT: TCRFTA at base of tongue

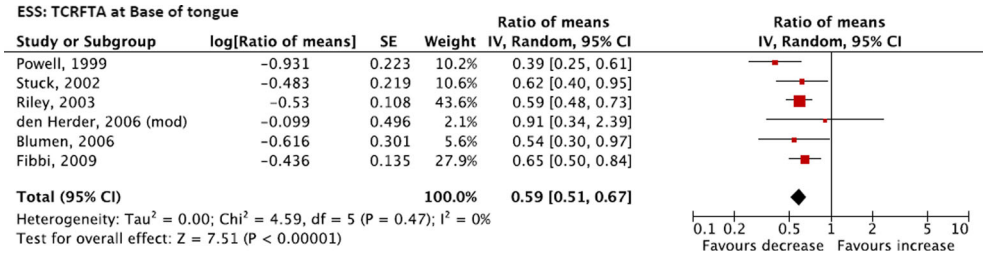

Fig. 4 ESS: TCRFTA at base of tongue

were quite limited but suggested that some of the improvements might wane with time. A recent meta-analysis [17], included primarily patients who were treated for snoring suggested that a reduction in snoring was maintained for over a year but truly long-term follow up was lacking and is essential before the true benefits of this therapy can be appreciated.

TCRFTA at soft palate

There was a paucity of studies examining TCRFTA of the soft palate alone. Other than an improvement in snoring, no significant short-term improvements could be found. Thus, based on the limited available data, TCRFTA of the soft palate alone appears to have limited efficacy. This result is not unexpected, as any improvement in obstruction at the level of the soft palate only may not be sufficient to significantly improve OSA. It is for this reason that ENT surgeons have moved towards multi-level TCRFTA. However, TCRFTA at the level of the soft palate may have some benefits in terms of reduction in snoring index and Epworth scores in habitual snorers without OSA [56]. However, a recent study examining long-term follow up for TCRFTA of the soft palate [18] found that snoring returned in most patients over time albeit its intensity was lower.

TCRFTA multi-level

There was a significant reduction in RDI after multilevel TCRFTA. However, significant heterogeneity was noted between studies. Two studies appeared to have better results than the remaining studies. The patients in these two studies were somewhat less obese than in the other studies and this might be responsible for the differing results. Racial differences seem an unlikely explanation as the two studies were from Thailand and Turkey, respectively. Thai and Turkish ancestry are very different, and this difference exceeds the difference between Turkish ancestry and the North American and European patients that make up the other studies, we reanalyzed the data excluding these studies and were reassured that the significant reduction in RDI remained. Oxygenation parameters were not significantly improved after TCRFTA. Sleepiness as measured by the ESS and VAS snoring both improved significantly post-TCRFTA, but heterogeneity between included studies was high. After exclusion of the aforementioned two studies causing heterogeneity in our results, a significant 22 % reduction in short-term mean ESS (RoM 0.78, 95 % CI 0.69–0.89, p=0.0001) and 46 % reduction in mean VAS snoring (RoM 0.54, 95 % CI 0.41–0.70, p<0.00001) was observed. Thus, multilevel TCRFTA resulted in both objective and subjective improvement in the short term. Again, long-term results are largely lacking. The sparse long-term data available suggests some diminution of response over time particularly if weight gain occurs (36). Similar to TCRFTA at base of tongue, there is considerable inter-subject variability with some subjects showing no improvement or even worsening after the procedure.

Study limitations The studies on which this meta-analysis is based were not of high methodological quality which lends caution to our conclusions. In particular, only 2 studies [52, 25] had a placebo control group. ESS and VAS snoring were the most frequently measured subjective measures. Disease specific quality of life questionnaires or other measures of sleepiness were not available for analysis. Generic quality of life measurements were available only in a few studies. Long-term outcome measurements were sorely lacking. Stratification of subjects by severity of sleep apnea and BMI could not be performed as only one study stratified responses based on the severity of sleep apnea [31] and no study stratified based on the BMI. Evaluating response rates based on an AHI below

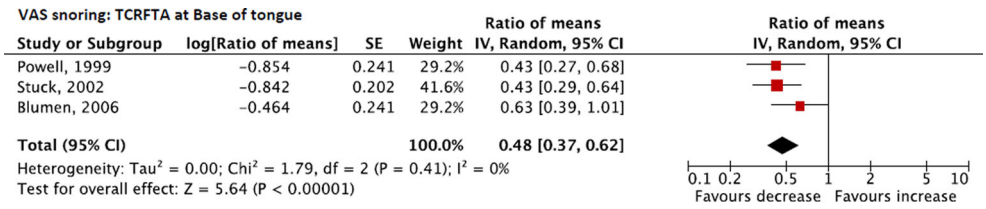

Fig. 5 VAS snoring: TCRFTA at base of tongue

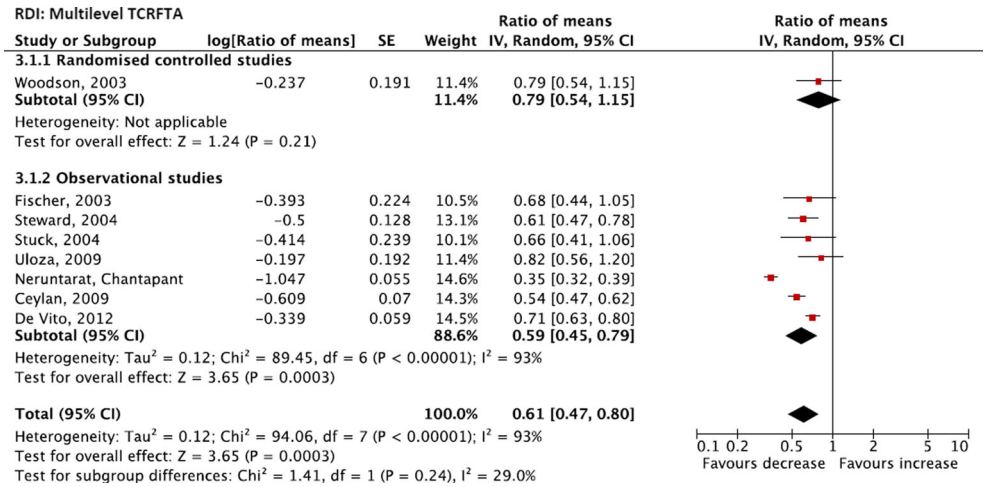

Fig. 6 RDI: multilevel TCRFTA (3.1.1 and 3.1.2)

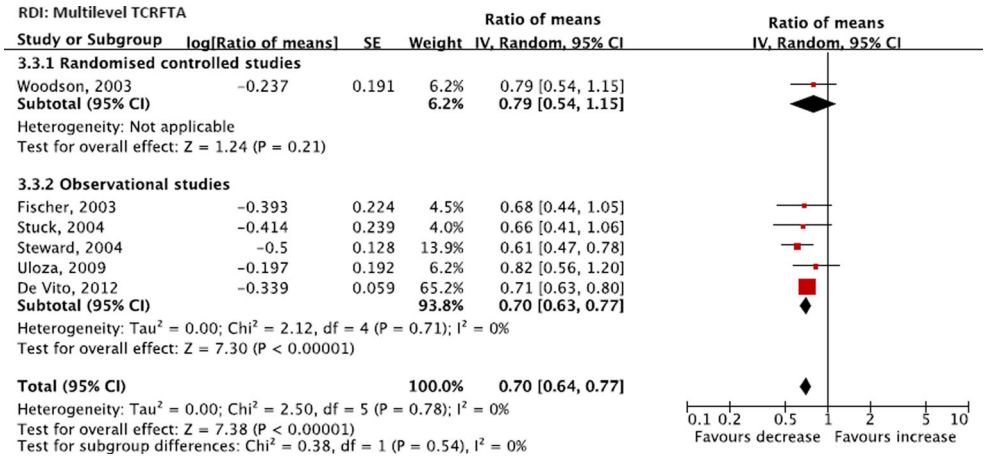

Fig. 7 RDI: multilevel TCRFTA (3.3.1 and 3.3.2)

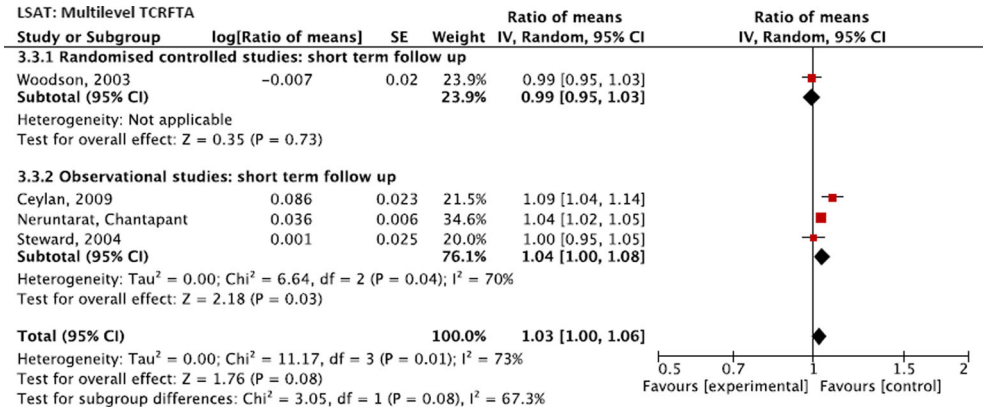

Fig. 8 LSAT: multilevel TCRFTA

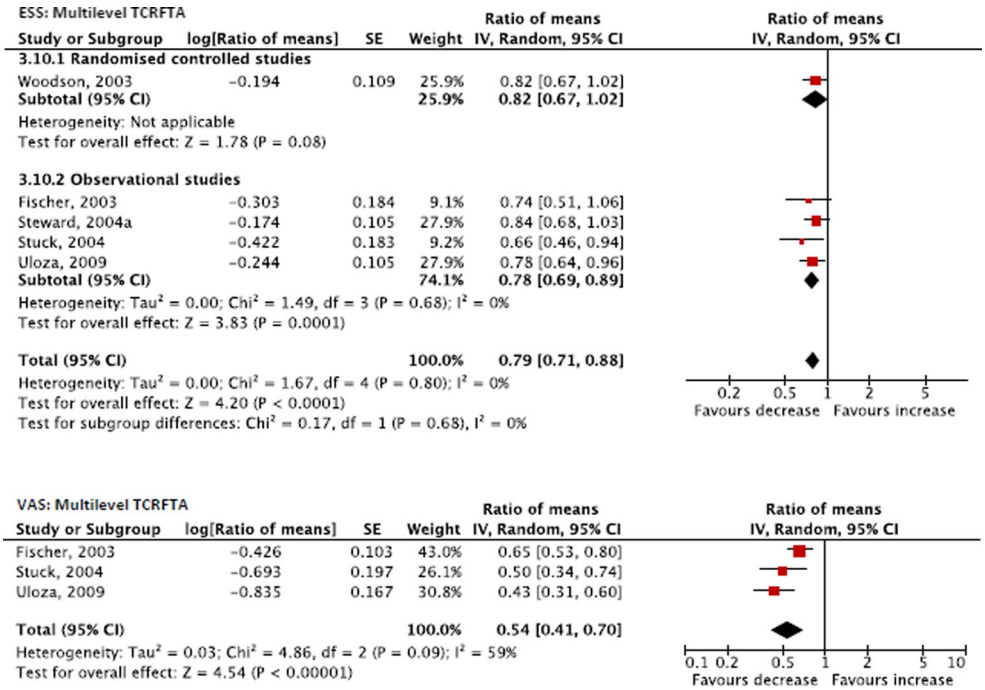

Fig. 9 ESS and VAS: multilevel TCRFTA

a threshold value (15, 10, or 5/hour) could not be performed as this information was provided in only 1 study [30]. In this study, none of the subjects (0/36) had an AHI less than 5/hour after TCRFTA. However, this may be too strict a criteria for surgical success. It would also have been helpful to study the role of PAP in patients who failed TCRFTA to see if prior TCRFTA adversely affected subsequent CPAP acceptance; however, this data was rarely provided. While analyzing data for Multi-level TCRFTA we failed to conclusively explain the heterogeneity generated by two trials and hence analyzed the data with and without them.

Clinical implications Temperature controlled radiofrequency tissue ablation appears to be an effective treatment option for OSA based on short-term follow up. Ablation at the base of the tongue or at multiple levels appears to be more efficacious than ablation at the level of the soft palate only. Complication rates were infrequent and rarely serious in nature. Patients with sleep apnea develop obstruction because of a small and more importantly a more collapsible upper airway. TCRFTA can increase upper airway size and the fibrosis produced may increase pharyngeal stiffness and reduce pharyngeal collapsibility. Pharyngeal collapse can occur at multiple sites in the upper airway so treatment at one site may not be sufficient to control sleep apnea. Patients are often reluctant to undergo staged multi-level surgeries to treat sleep apnea. TCRFTA can allow a multi-level approach at a single sitting and the procedure can be easily repeated to achieve the desired result. This makes TCRFTA potentially quite attractive as a stand-alone therapy for OSA in patients intolerant to CPAP. Long-term follow-up studies and better data on short-term cure rates (percentage of patients who have an AHI below a defined threshold (10 or 15/hour) are needed before this procedure can be confidently added to the treatment armentarium for sleep apnea.

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Conflict of interest None

Financial disclosures None

Appendix 1

Search terms used included medical subject headings and the keywords "Catheter Ablation," "Diathermy," "Electrocoagulation," "Sleep Apnea Syndrome," "Sleep Apnea, Obstructive," "Sleep disordered breathing," and "Submucosal Radiofrequency Tongue Ablation" limited to humans. The most recent search was conducted in April 2013.

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