

Technologic Advances in the Treatment of Obstructive Sleep Apnea Syndrome*

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Among adult patients with obstructive sleep apnea syndrome (OSAS), adherence to continuous positive airway pressure (CPAP) treatment is approximately 40%, according to recent well-designed studies that evaluated outcomes other than adherence as a primary end point. This finding suggests the need for the improvement of the adult OSAS treatment approach, either by improving adherence to CPAP treatment or by developing effective alternatives to CPAP. Technologic advances have allowed for the development of new treatments for OSAS that include automatic CPAP and innovative airway procedures. Studies evaluating the application of these new technologies are reviewed. These technologic advances can be viewed as possible improvements over the existing treatment approach only if the risks and benefits of each new treatment are well understood by OSAS patients and their physicians.

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Key words: automatic continuous positive airway pressure; hypoglossal nerve stimulator; obstructive sleep apnea syndrome; upper airway resistance syndrome; uvulopalatopharyngoplasty

Abbreviations: AHI = apnea-hypopnea index; CAPSO = cautery-assisted palatal stiffening operation; CPAP = continuous positive airway pressure; LAUP = laser-assisted uvulopalatoplasty; OSAS = obstructive sleep apnea syndrome; PSG = nocturnal polysomnography

The prevalence of obstructive sleep apnea syndrome (OSAS) in the United States is 2 to 4% in middle-aged adults,¹ which is similar in magnitude to the prevalence of some diseases considered to be major public health issues, such as diabetes mellitus or asthma. Preliminary studies suggest an association between untreated OSAS and an increased risk for cardiovascular disease, especially hypertension.² The Sleep Heart Health Study and other ongoing cardiovascular outcome studies should provide guidance on the strength of these associations and determine whether OSAS contributes an independent risk.³ In lieu of these pending data, the most important and well-established consequences of untreated OSAS include impaired vigilance,⁴ decreased quality of life,⁵ and increased risk for motor vehicle accidents.⁶ The future treatment approach to adult OSAS will be tempered by the results of these ongoing cardiovascular outcomes studies with respect to the appropriateness of more complex and expensive treatment options, including those discussed in this review

article: automatic continuous positive airway pressure (CPAP) and innovative upper airway procedures.

Recent randomized, controlled trials of CPAP vs placebo⁷ or conservative treatment⁸ of OSAS demonstrate improvement of daytime sleepiness and quality-of-life measures in the CPAP-treated cohorts. However, these CPAP treatment trials also determined that adherence to this therapy is approximately 40%, suggesting that there is a need to improve CPAP therapy or develop effective treatment alternatives. This review scrutinizes (1) the innovations in OSAS treatment, including automatic CPAP, that could allow for improved CPAP adherence, and (2) pharyngeal surgeries and nerve stimulators, which might provide an effective alternative to CPAP. The mechanics, efficacy, side-effect profile, and cost considerations are discussed for each of these treatment modalities.

AUTOMATIC CPAP

Mechanisms

During the last decade, at least eight self-adjusting CPAP systems have been developed and utilized to treat adult OSAS patients, either for the unattended titration of CPAP or for long-term variable pressure treatment. Because these systems function by recog-

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nizing obstructive respiratory events or surrogate measures of them, the systems have an inherent diagnostic capability. The accuracy of the diagnostic capabilities, as well as the characteristics of the internal algorithms for pressure adjustment, are key components of the efficacy and patient acceptability of these systems. The level of technical sophistication and associated monetary costs of these systems may vary greatly, and each system requires individualized and careful evaluation before use in OSAS patients is advocated or discouraged.

Parameters monitored by the various systems include those derived from airflow, pressure, or snoring and other airway sounds. One example of an automatic CPAP system, AutoAdjust (DeVilbiss Health Care, Inc; Somerset, PA), uses a pneumotachometer to measure airflow and calculates a running average by either machine default or user-specified event definitions based on time and percentage of flow decrement.⁹ AutoSet (ResMed; San Diego, CA) increases mask pressure in response to apneas, breath-to-breath flattening of inspiratory airflow waveform contour, or snoring (Fig 1).¹⁰ Morphée Plus (Pierre Medical; Verrieres le Buisson Cedex, France) utilizes a user-specified reference pressure, and the effective pressure varies on the basis of peak inspiratory and expiratory airflow based on machine compressor speed.¹¹ Virtuoso (Respiron-

ics Inc; Murrysville, PA) increases mask pressure in response to airway vibration patterns as sensed by a pressure transducer.¹²

Diagnostics

Few of the automatic CPAP systems have been evaluated with respect to diagnostic capabilities. An exception to this lack of validation is the AutoSet CPAP device, which was evaluated in the diagnostic mode in four studies with simultaneous nocturnal polysomnography (PSG). Overall, correlations were robust for the apnea index (mean number of apneas/h) and apnea-hypopnea index (mean number of apneas and hypopnea/h [AHI]) in studies by Bradley et al,¹³ Gugger et al,¹⁴ and Fleury et al¹⁵; however, for patients with an AHI of < 15, there was poor agreement between AutoSet and PSG. In approximately 10% of OSAS patients, large-magnitude discrepancies between the AHIs were attributed to inadequate airflow related to increased oral breathing and displaced nasal pressure transducer position. A recent study by Rees et al¹⁶ of 20 patients with severe OSAS determined that the AutoSet underdetected hypopneas during sleep by 41% and that 20% of the apneas and hypopneas detected occurred during wakefulness. Based on the data available for the current obstructive event-sensing algorithm for

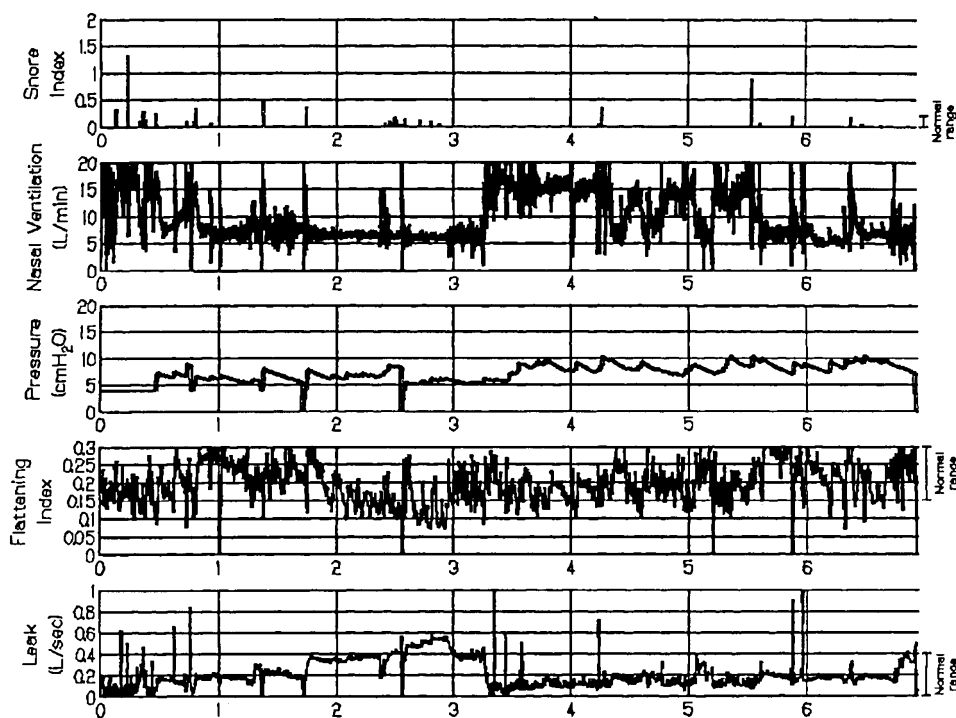


FIGURE 1. Example of cumulative overnight automatic CPAP data report for a patient with severe OSAS. Used with permission of ResMed Corporation.

AutoSet, it is likely that patients with severe OSAS can be accurately identified from a population of suspected OSAS patients. Whether mild or moderate OSAS patients can be distinguished from patients with other sleep disorders with AutoSet or any other system has not been well evaluated to date.

Titration

The majority of peer-reviewed studies on the various commercially available automatic CPAP systems suggest that OSAS treatment in the sleep laboratory environment results in final CPAP settings comparable to those obtained in technician-titrated studies with PSG.^{17–21} This finding may have economic value in allowing for a decrease in the technician-to-patient ratio in the sleep laboratory and thereby reducing costs.²² However, it has not been established that unattended automatic CPAP titration is safe without a previous diagnostic PSG to establish the diagnosis of OSAS and exclude patients with additional overlap or non-OSAS nocturnal breathing disorders. Non-OSAS nocturnal breathing disorders include central sleep apnea or chronic hypoventilation due to emphysema or other diseases. A single case report documents the occurrence of iatrogenic central sleep apnea induced by automatic CPAP in an OSAS patient.²³ Another potential hazard is unrecognized arrhythmia during CPAP titration, although its occurrence has been documented in only a single case series.²⁴ Future versions of automatic positive airway pressure systems may allow for the recognition and appropriate treatment of non-OSAS breathing disorders²⁵ or arrhythmia, but these systems are not yet developed or available clinically.

Without a technician in attendance, OSAS patients are at risk for intermittent or continuous mask leak during a titration study, which may lead to increased variability of CPAP pressures and associated arousals. This risk may be decreased by close attention to mask fit and by educating the patient about mask self-adjustment techniques prior to the titration study.²⁶ Whether an accurate final CPAP prescription can be obtained with automatic CPAP in a home environment has not been well studied. Because some automatic CPAP systems may allow for the measurement and recording of mask leak, inadequate airflow or pressure signals, and other sources of artifact, inadequate titration can be recognized and the appropriate adjustments made to allow for repeat home titration or technician-supervised titration. The effect of home automatic CPAP titration on treatment acceptance and adherence are unknown, but considering the well-documented poor adherence rates for CPAP when OSAS patients are

not closely supervised and intensively educated,^{7,8} there is significant risk for even further decrease in adherence rates if physician and technician contact are minimized.

Compensation issues may be critical to the clinical utilization of new technologies including automatic CPAP. In the United States, Medicare and most third-party payers currently will not reimburse for either attended or unattended automatic CPAP titration studies. The future trend may be for the automatic CPAP manufacturers to add additional diagnostic recording capabilities to these systems to allow for compensation as an attended cardiorespiratory (four-channel) study monitoring airflow, respiratory effort, oxygen saturation, and heart rate. Expanding the diagnostic capabilities of automatic CPAP titration systems could allow for effective home titration of CPAP with continuous technician monitoring and intervention through a centralized hub. A feasibility study by Coppola and Lawee²⁷ determined that 11 closely followed OSAS patients could self-titrate CPAP at home without complication. A number of managed-care organizations have implemented programs using screening algorithms and nocturnal cardiorespiratory monitoring to diagnose OSAS, followed by unattended, home CPAP titration studies for those who screen positive.²⁸ Widespread application of this approach cannot be advocated without systematic, peer-reviewed studies that demonstrate acceptable diagnostic accuracy of this approach compared with the gold standard, PSG, and assess treatment efficacy utilizing objectively measured outcomes such as machine-monitored CPAP adherence.

Variable Pressure

For severe OSAS patients identified by prior PSG, the home use of a number of the automatic CPAP systems in the variable-pressure mode result in lower overnight cumulative CPAP levels compared with CPAP at a preset, fixed level.²⁶ Studies of the AutoAdjust,⁹ AutoSet,²⁹ and Morphée Plus¹¹ demonstrate that use of variable-pressure CPAP resulted in decreases in the AHI that were the same as those attained with technician-titrated CPAP. Preliminary data suggest that specific automatic CPAP systems may vary with respect to efficacy in the reduction of AHI for OSAS treatment.³⁰ Only one preliminary study evaluated automatic CPAP treatment in adult upper airway resistance syndrome, which is defined by increased inspiratory driving pressure detected by esophageal manometry during sleep without evidence of airflow limitation by oronasal thermistor.³¹ This study determined that the AutoSet reduced the number of respiratory effort-related arousals

(38.3 ± 20 /h pretreatment vs 7.1 ± 4.8 /h posttreatment; $p = 0.005$), but that the residual driving pressure was increased in OSAS patients treated with the Autoset compared with matched patients treated with technician-titrated CPAP.³²

A comparison of sleep architecture in the home environment for variable pressure and conventional CPAP has not been done, but in-laboratory comparisons suggest that there are no consistent differences for any specific system.³³ Few studies have evaluated long-term adherence (> 2 months) with automatic CPAP, although Konermann et al,²⁰ in a crossover study of 50 OSAS patients, found an increase in the mean treatment nights per week but no increase in the mean hours of usage per night. Whether the added expense of a variable CPAP capability is justified with respect to patient comfort and adherence benefits remains to be determined by future studies. Subgroups of OSAS patients who are more or less likely to benefit from automatic CPAP have not been identified. Automatic CPAP is more expensive than fixed-pressure CPAP. The added cost varies for each system, but some systems may cost less than \$500 more than fixed-pressure CPAP systems. Currently, few third-party payers in the United States routinely authorize reimbursement for the added cost of automatic CPAP for home use.

UPPER AIRWAY PROCEDURES

Palatal Surgery

Surgery on the soft palate to treat OSAS has previously been performed using a scalpel (uvulopalatopharyngoplasty [UPPP]).³⁴ More recently, procedures have involved with CO₂ or YAG lasers (laser-assisted uvulopalatoplasty [LAUP]),³⁵ cautery (cautery-assisted palatal stiffening operation [CAPSO]),³⁶ or radiofrequency energy (Somnoplasty; Somnus; Mountainview, CA).³⁷ An advantage of LAUP, CAPSO, and Somnoplasty over UPPP is that these procedures are performed with local anesthesia, and thus are adaptable to an ambulatory setting.

The fundamental shortcoming of all palatal surgical procedures to date, including the newer techniques, is that the majority of OSAS patients are inadequately treated on the basis of reduction in the AHI. In a study by Doghramji et al³⁸ of 53 OSAS patients identified by awake endoscopy as palatal obstructors on the basis of the Muller maneuver, only 32% of these severe OSAS patients (mean AHI, 46.5) demonstrated a $\geq 50\%$ decrease in AHI with UPPP. Results from LAUP studies suggest even less clinical utility than UPPP for OSAS treatment, although selection bias related to lack of posttreatment

PSG has resulted in a wide variance in changes in the AHI as reported in the otolaryngology literature.^{39–41} The failure of LAUP in the treatment of OSAS has been attributed to the limited resection of pharyngeal tissue compared with UPPP. Modification of the LAUP procedure to include more complete resection of the pharynx was proposed by Mickelson and Ahuja⁴² in a recent study, in which only 36 of 59 OSAS patients (61%) underwent posttreatment PSG. These authors' conclusion that a more aggressive LAUP procedure is "an effective treatment for mild, moderate and severe" OSAS is doubtful in view of the previously reported limited efficacy rate of UPPP and potential selection bias in the current study.

Novel palatal stiffening procedures include CAPSO and Somnoplasty. Palatal tissue is not excised or ablated as with UPPP or LAUP, but rather, a midline soft palate scar forms within 1 to 2 months following CAPSO or Somnoplasty. With respect to the effect of these novel palatal procedures on AHI for OSAS patients, only data in abstract form are available for CAPSO,³⁷ and a multicenter clinical trial is ongoing to evaluate palatal Somnoplasty. An advantage of Somnoplasty over other palatal procedures may be decreased pain due to the avoidance of mucosal tissue resection; however, repetition of the procedure is usually required before the optimal surgical effect is obtained, which leads to increased cost.⁴³ Palatal mucosal tissue is excised from the midline with CAPSO, and although the procedure is of short duration and is inexpensive, postoperative pain is considerable and could preclude further study of this procedure.

In summary, palatal procedures alone are not likely to be effective for the majority of OSAS patients, no matter which technique is used. To date, no studies guide the selection of patients more likely to benefit from these procedures, except possibly for those with mild severity based on AHI. As discussed below, it is necessary that additional surgical procedures be available to allow for the salvaging of palatal surgery failures.

Tongue Base Procedures

Since 1981, Riley and Powell of Stanford University have developed a stepwise approach to the surgical treatment of OSAS. Patients in whom UPPP has failed may undergo subsequent surgery such as geniohyoid advancement myotomy combined with hyoid resuspension and/or (in a smaller subset of patients) maxillomandibular advancement. As with much of the palatal surgery outcome literature, the Stanford surgical OSAS treatment data are flawed by potential selection bias, with a 26% loss to follow-up

in a retrospective study of 415 adult OSAS patients published in 1993.⁴⁴ However, smaller studies of consecutive patients receiving these procedures⁴⁵ suggest that surgical treatment of OSAS is more effective than palatal surgery alone, especially with maxillomandibular advancement.⁴⁶ Unfortunately, while palatal surgery is widely available, relatively few surgeons perform these additional procedures for the treatment of OSAS patients. Advanced surgical expertise is required to perform these additional procedures, and prolonged hospitalization and high costs are associated with such procedures, especially maxillomandibular advancement. Although no studies have evaluated this issue, it is assumed that high numbers of OSAS patients who fail palatal surgery remain untreated.

Novel procedures for OSAS that persists after palatal surgery address obstruction at the base of tongue; options include suture suspension with the Repose System (Influence Corp; San Francisco, CA) and Somnoplasty. The results of prior attempts at scalpel or laser resection of the tongue base in OSAS treatment have not been good enough to recommend continued application of these procedures. In a 1997 study by Mickelson and Rosenthal,⁴⁷ only 3 of 12 patients who received laser tongue base resection had a posttreatment AHI of < 20 . Although no intraoperative complications were reported, the mean hospital stay after this procedure was 3.6 days, and 50% of the patients required temporary tracheotomy. It is likely that the Repose and Somnoplasty base-of-tongue procedures offer an advantage over prior base-of-tongue resection and other nonpalatal procedures in that these newer procedures are easier to perform and are associated with shorter or no hospital stays.

The Repose procedure is performed under gen-

eral anesthesia, and a screw is inserted at the base of the mandible. The screw contains attachments for polypropylene suture that is passed through the tongue base, allowing for anterior support (Fig 2). Tightness of the tongue suspension is determined digitally, and caution must be exercised to prevent tissue ischemia, pain, and edema. In a study of 16 carefully selected OSAS patients who had not undergone palatal surgery, PSG 3 months after treatment demonstrated a decrease in the AHI from 35 ± 8 to 17 ± 8 ($p = 0.001$).⁴⁸ Only 1 of 15 patients (7%) demonstrated a posttreatment AHI of ≤ 10 and a $> 50\%$ reduction from the pretreatment AHI (Fig 3). Two patients had postoperative pain and local soft tissue infection requiring removal of the tongue base suture and exclusion from the treatment data analysis. An additional patient developed a floor-of-mouth cyst requiring marsupialization. Another case series evaluated this procedure in 72 OSAS patients with prior palatal surgery⁴⁹; approximately 10% of patients were not evaluated postoperatively with PSG. Hyoid suspension and myotomy were concomitantly performed in 24 of the 72 patients, but the selection criteria for this additional procedure were not specified. With the Repose procedure alone, the AHI decreased from 65 ± 21 to 45 ± 17 (31%); in combination with hyoid surgery, the AHI decreased more markedly, from 74 ± 19 to 30 ± 16 (59%). Short-term complications included temporary odynophagia and dysphagia, but all patients were able to tolerate liquids and a soft diet by time of discharge after a mean hospital stay of 1.2 days; the base-of-tongue suture was not removed in any patient.

Base-of-tongue Somnoplasty is performed under local anesthesia in an outpatient setting. Radiofrequency energy is delivered via a needle electrode to

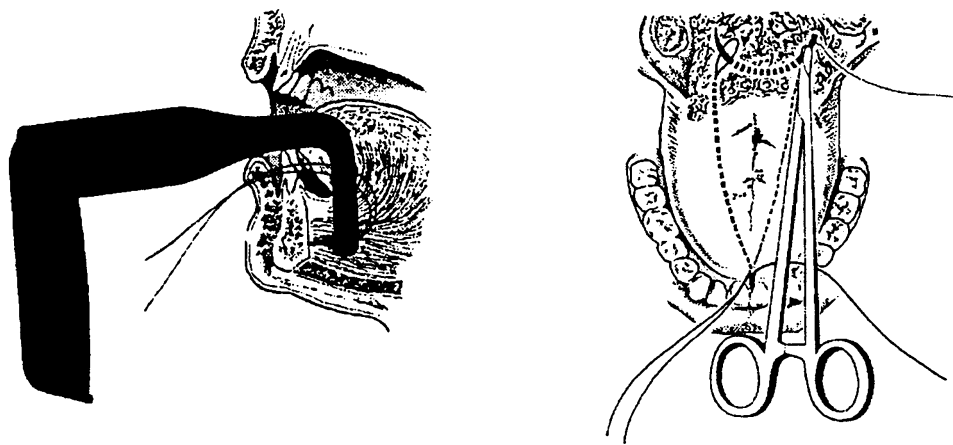


FIGURE 2. Depiction of screw placement in the mandible and suture placement with base of tongue resuspension. Used with permission of Influence Corporation.

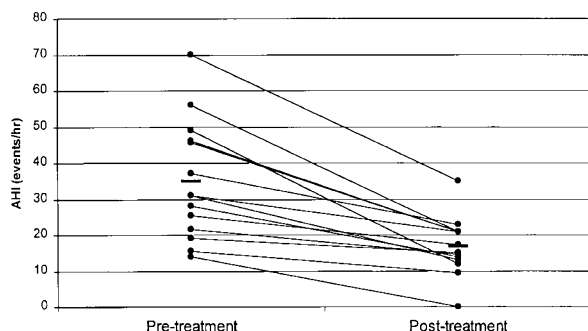


FIGURE 3. Change in the AHI in a cohort of OSAS patients who underwent base-of-tongue suture resuspension. Based on data from DeRowe et al.⁴⁸

the midline at the anterior junction of the anterior two thirds of the tongue and posterior base, creating a coagulative lesion in the muscle with resultant fibrosis over time. In 20 OSAS patients who had previously undergone palatal procedures, a mean of five repeat radiofrequency base-of-tongue procedures were performed approximately every 4 weeks, delivering a mean energy total of 8,490 J per patient. The AHI decreased from 40 ± 32 to 18 ± 16 ($p = 0.003$) with this series of procedures, although two patients (11%) did not undergo posttreatment PSG.⁵⁰ Individual patient data were remarkable in that three of the patients did not have pretreatment OSAS, as defined by an AHI of > 5 , and 5 of 15 patients (33%) demonstrated a posttreatment AHI of ≤ 10 and a $> 50\%$ reduction from the pretreatment AHI (Fig 4). MRI demonstrated a 17% reduction in tongue volume after the series of procedures were complete. Three patients experienced adverse events, including a superficial tongue ulceration and a soft tissue infection that required incision and drainage under general anesthesia and a temporary tracheotomy. Costs for this technique are increased by the need for multiple procedures: the current

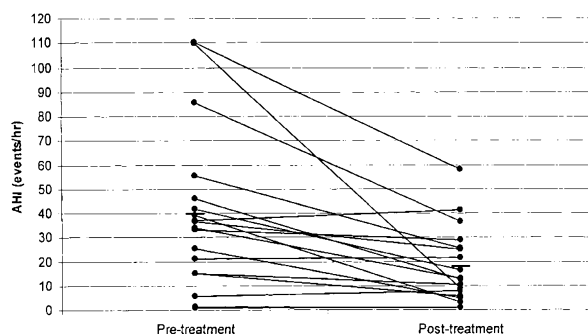


FIGURE 4. Change in the AHI in a cohort of OSAS patients who underwent base-of-tongue radiofrequency ablation. Based on data from Powell et al.⁵⁰

version of the radiofrequency needle and handle assemblage are not reusable.

Implanted Electrical Nerve Stimulation

Studies of anesthetized animals⁵¹ and humans⁵² demonstrate that stimulation of the hypoglossal nerve results in activation of the genioglossus muscle and subsequent tongue protrusion, with increases in pharyngeal diameter and flow. Schwartz et al⁵³ of the Johns Hopkins University completed a study of eight patients with severe OSAS. The authors determined that implanted single-hook wire stimulation of the hypoglossal nerve during unanesthetized sleep could be performed for an unspecified time interval with resultant increased flow and no increase in the frequency of associated arousals. Four of these sleeping OSAS patients were also monitored for a mean of 22 min, during which determination of increased pharyngeal resistance by pressure manometry and pneumotachometer was used to trigger nerve stimulation. A multicenter clinical trial of the feasibility of a hypoglossal nerve stimulator (Inspire System; Medtronic, Inc; Minneapolis, MN) for the treatment of OSAS is in the preliminary phase, but progress has been slowed by technical issues. The concept of nerve stimulation remains an attractive conceptual alternative to CPAP, but much technologic and clinical work will be required before this novel OSAS treatment can be considered for widespread use. The initial costs for an impulse generator and lead implantation pose a significant barrier for the clinical application of this technology in OSAS treatment, although cost-effectiveness cannot easily be assessed without definitive cardiovascular outcome data from ongoing prospective OSAS epidemiologic studies.

CONCLUSION

It is hoped that these novel technologies and procedures will lead to the improved efficacy and tolerability of OSAS treatment. However, caution is advised because, despite the preliminary nature of much of the related research, the relative ease of applying some of these technologies and performing some of these novel procedures may result in widespread use. Evaluation of some of the specific OSAS technologies or procedures in the past has been problematic because of study selection bias and a lack of control or comparison groups. More systematic research efforts in the future should allow for accurate assessments of innovative treatments and optimize their refinement and integration into the clinical management of OSAS.

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