Advances in Diagnosis and Treatment of Sleep Apnea Syndrome in Japan

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Abstract

The complaint of excessive daytime sleepiness (EDS) by patients with severe sleep apnea syndrome (SAS) represents an alarming sign for the risk of accidents caused by drowsy driving. Obstructive SAS (OSAS) is closely associated with lifestyle-related diseases and metabolic syndrome resulting from obesity, and is frequently accompanied by hypertension, dyslipidemia, and impaired glucose tolerance. Furthermore, it has become clear that patients with OSAS are likely to have cardiovascular disease, stroke, and chronic kidney disease (CKD). For these reasons, the diagnosis and treatment of sleep-disordered breathing (SDB) with particular focus on SAS should be further expanded among general clinicians in Japan. We reviewed the diagnostic and treatment algorisms for SDB and the guidelines for clinical collaboration in SDB, which we developed as part of the cooperative study under the fiscal 2005–2007 Research Grant (20B-4) for Nervous and Mental Disorders from the Ministry of Health, Labour and Welfare (Chief Researcher: Tetsuo Shimizu).

Key words Sleep apnea, Sleep-disordered breathing, Metabolic syndrome, Cardiovascular disease

Introduction

The incident caused by drowsy driving on the West Japan Railway Company's Sanyo Shinkansen Line in February 2003 highlighted the important problem that the train's driver with sleep apnea syndrome (SAS) had the subjective symptom of excessive daytime sleepiness (EDS) rather than the long-recognized objective symptom of snoring. A survey of 2,174 SAS patients hospitalized for examination at the Sleep Disorders Center, Aichi Medical University Hospital revealed that 232 patients (10.7%) had caused traffic accidents due to drowsy driving of automobiles during the preceding 5 years.[1] In a severe case of SAS, the patient's complaint about EDS is a warning sign of possible accidents caused by drowsy driving. On the other hand, SAS is closely associated with lifestyle-related diseases and metabolic syndrome resulting from obesity, and is frequently accompanied by cardiovascular diseases, such as hypertension, ischemic heart disease, arrhythmias, and heart failure, and also tends to be accompanied by stroke and chronic kidney disease (CKD)[2–4] (Fig. 1).

We reviewed the diagnosis and treatment in Japanese patients with SAS, focusing on the recent publication of "the Guidelines for Diagnosis, Treatment, and Clinical Collaboration in Sleep-Disordered Breathing."[5]

Diagnostic Classifications in SAS and SDB

SAS is classified into 4 types: obstructive, central, mixed, and complex. When we talk about SAS, it usually refers to obstructive SAS (OSAS), which is the most prevalent type. According to the criteria defined by the American Academy of Sleep Medicine (AASM), OSAS is a medical condition presenting the various symptoms caused by EDS

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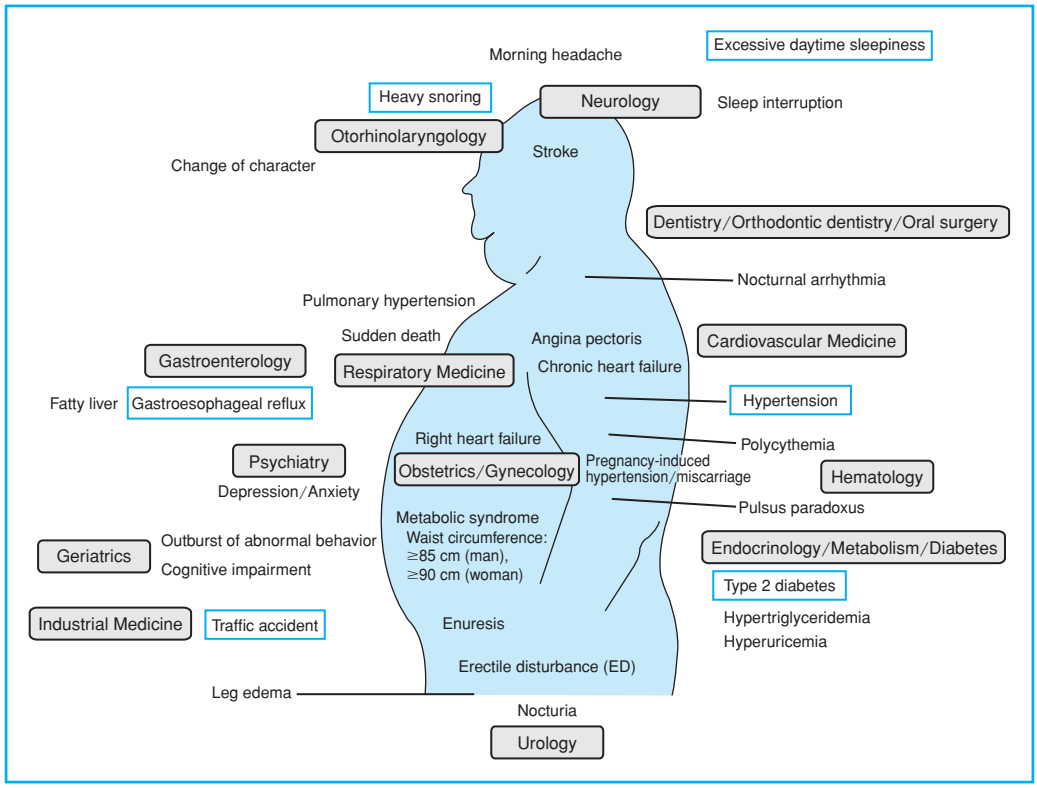


Fig. 1 Diverse clinical symptoms of the sleep apnea syndrome (SAS) and clinical departments

Table 1 Classification of sleep-disordered breathing (SDB)

Central sleep apnea syndromes
Primary central sleep apnea
Central sleep apnea due to Cheyne stokes breathing pattern
Central sleep apnea due to high-altitude periodic breathing
Central sleep apnea due to medical condition not Cheyne stokes
Central sleep apnea due to drug or substance
Primary sleep apnea of infancy (formerly primary sleep apnea of newborn)
Obstructive sleep apnea syndromes
Obstructive sleep apnea, adult
Obstructive sleep apnea, pediatric
Sleep related hypoventilation/hypoxemic syndromes
Sleep related nonobstructive alveolar hypoventilation, idiopathic
Congenital central alveolar hypoventilation syndrome
Sleep related hypoventilation/hypoxemia due to medical condition
Sleep related hypoventilation/hypoxemia due to pulmonary parenchymal or vascular pathology
Sleep related hypoventilation/hypoxemia due to lower airways obstruction
Sleep related hypoventilation/hypoxemia due to neuromuscular and chest wall disorders
Other sleep related breathing disorder
Sleep apnea/sleep related breathing disorder, unspecified

(American Academy of Sleep Medicine: ICSD-2, 2005.)

Table 2 Diagnostic criteria for obstructive sleep apnea, adults

A, B and D or C and D satisfy the criteria

A. At least one of the following applies:
   1. The patient complains of unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, fatigue, or insomnia.
   2. The patient wakes with breath holding, gasping, or choking.
   3. The bed partner reports loud snoring, breathing interruptions or both during the patient's sleep.

B. Polysomnographic recording shows the following:
   1. Five or more scoreable respiratory events (i.e., apnea, hypopneas, or RERAs) per hour of sleep.
   2. Evidence of respiratory effort during all or a portion of each respiratory event (In the case of a RERA, this is best seen with the use of esophageal manometry.)

or

C. Polysomnographic recording shows the following:
   1. Fifteen or more scoreable respiratory events (i.e., apneas, hypopneas, or RERAs) per hour of sleep.
   2. Evidence of respiratory effort during all or a portion of each respiratory event. (In the case of a RERA, this is best seen with the use of esophageal manometry.)

D. The disorder is not better explained by another sleep disorder, medical or neurological disorder, medication use, or substance use disorder.

(American Academy of Sleep Medicine (AASM): ICSD-2, 2005.)

Severity criteria
Mild: 5 or 15 events per hour.
Moderate: 15 to 30 events per hour.
Severe: greater than 30 events per hour.

[AASM Task Force (1999), Chicago criteria.]

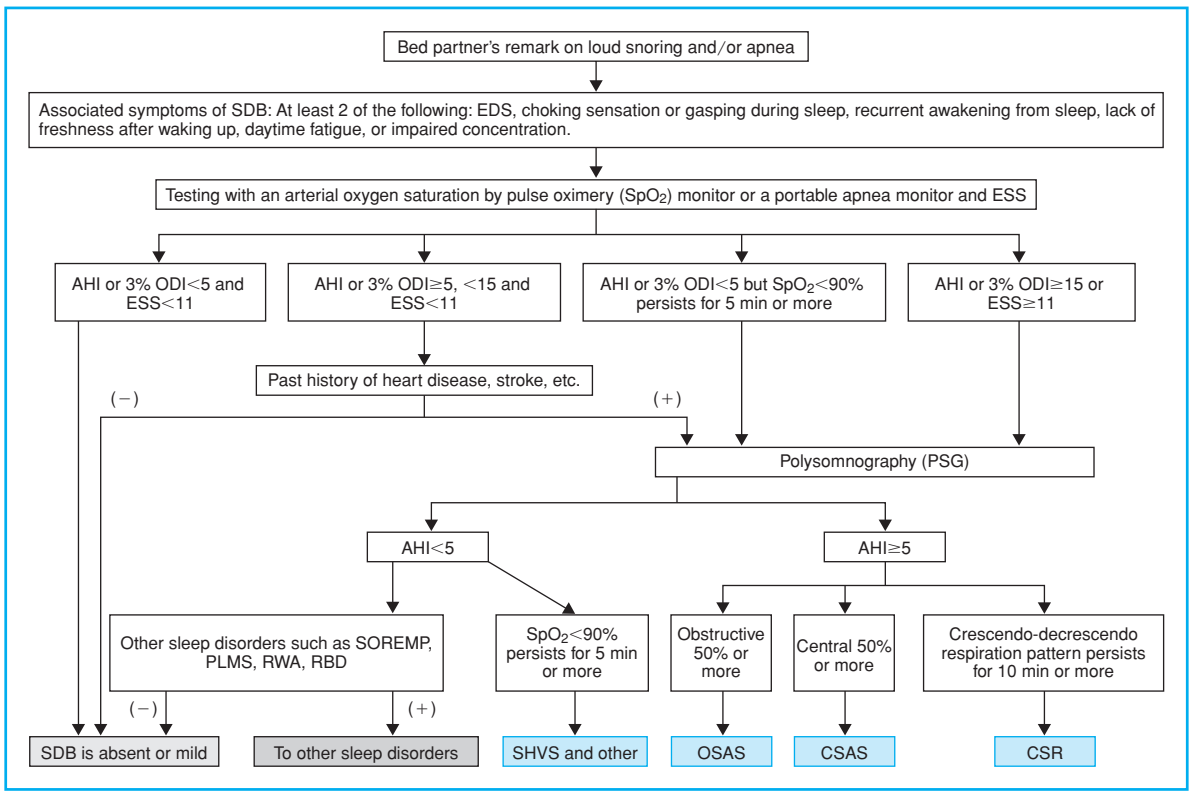
and obstructive sleep apnea (OSA) with an apnea-hypopnea index (AHI) of 5 or more.[6,7] However, aside from OSAS, there are many pulmonary and cardiovascular diseases that develop or aggravate in relation to sleep. These are collectively called sleep-related breathing disorders or sleep-disordered breathing (SDB).

Table 1 shows the diagnostic classification of SDB in the International Classification of Sleep Disorders, Second Edition (ICSD-2).[8] Here, it should be understood that OSAS is part of the complex pathologic entity called SDB.

Guidelines for Diagnosis and Treatment of SAS

Table 2 shows the ICSD-2 diagnostic criteria for OSAS in adults.[8] Similar guidelines were also published in Japan. The Sleep-Disordered Breathing Society in collaboration with 5 related academic societies developed "The Guidelines for Diagnosis and Treatment of Sleep Apnea Syndrome in Adults" in 2005 as a guide for general clinicians treating OSAS.[6] Guidelines were also formulated for more specific purposes, including "The Manual for the Treatment of Sleep-Disordered Breathing (Snoring and the Sleep Apnea Syndrome)"[9] for otolaryngologists and "The Treatment of the Sleep Apnea Syndrome in Dentistry under Health Insurance—Collaboration between Medical and Dental Care"[10] developed with the participation of the Health Insurance Dental Care Society, but there are no guidelines targeted at children and seniors yet.

Because of the high rate of central SAS (CSAS) accompanying chronic heart failure (CHF), the coverage of the national health insurance system was expanded to include home oxygen therapy (HOT) in 2004 and adaptive pressure support servo-ventilation (ASV) in 2007 for CHF patients with Cheyne-Stokes respiration (CSR). Within the Japanese Circulation Society, "The Guidelines for Diagnosis and Treatment of Sleep-Disordered Breathing in Cardiovascular Medicine" Development Team (Head: Shinichi Momomura) has been working to develop guidelines since fiscal 2008.[11–13]



(Shiomi T, et al.: The Guidelines for Diagnosis, Treatment, and Clinical Collaboration in Sleep-Disordered Breathing. The fiscal 2005–2007 report of "The Study Regarding the Development of Guidelines for the Construction of National Medical Care Network for Sleep Disorders (Chief Researcher: Tetsuo Shimizu)" under the Research Grant for Nervous and Mental Disorders from the Ministry of Health, Labour and Welfare, 2008; 13–21.)

Fig. 2 Diagnostic algorism for sleep-disordered breathing (SDB)

The Guidelines for Diagnosis, Treatment, and Clinical Collaboration in SDB

The great complexity of the manifestations of SDB other than OSAS makes it necessary that the medical intervention for SDB be supported by the collaboration among physicians and dentists from diverse specialties such as internal medicine (cardiology, pneumology, endocrinology/metabolism/diabetes, neurology, etc.), otolaryngology, dentistry/oral surgery, and psychiatry (inter-department collaboration). It was therefore necessary to develop comprehensive guidelines also including regional medical collaboration. To this end, an SDB diagnosis and treatment algorism was developed in "The Study Regarding the Development of Guidelines for the Construction of National Medical Care Network in Sleep Disorders (Chief Researcher: Tetsuo Shimizu)" under the fiscal 2005–2007 Research Grant for Nervous and Mental Disorders from the Ministry of Health, Labour and Welfare as part of the cooperative research regarding the guidelines for diagnosis, treatment, and clinical collaboration in SDB (Figs. 2 and 3).[5]

The Guidelines for Diagnosis, Treatment, and Clinical Collaboration in SDB[5] state that general medical institutions (general clinicians) should appropriately diagnose patients with symptoms such as EDS and snoring and suspected of having SDB, and that the patients requiring more advanced diagnosis and treatment should be referred to specialized medical institutions with expertise in sleep medicine (specialized sleep disorders institutes). These institutes such as the medical institutions accredited by the Japanese Society of Sleep Research provide appropriate diagnosis and treatment of sleep disorders in general, including the definitive diagnosis of SDB.

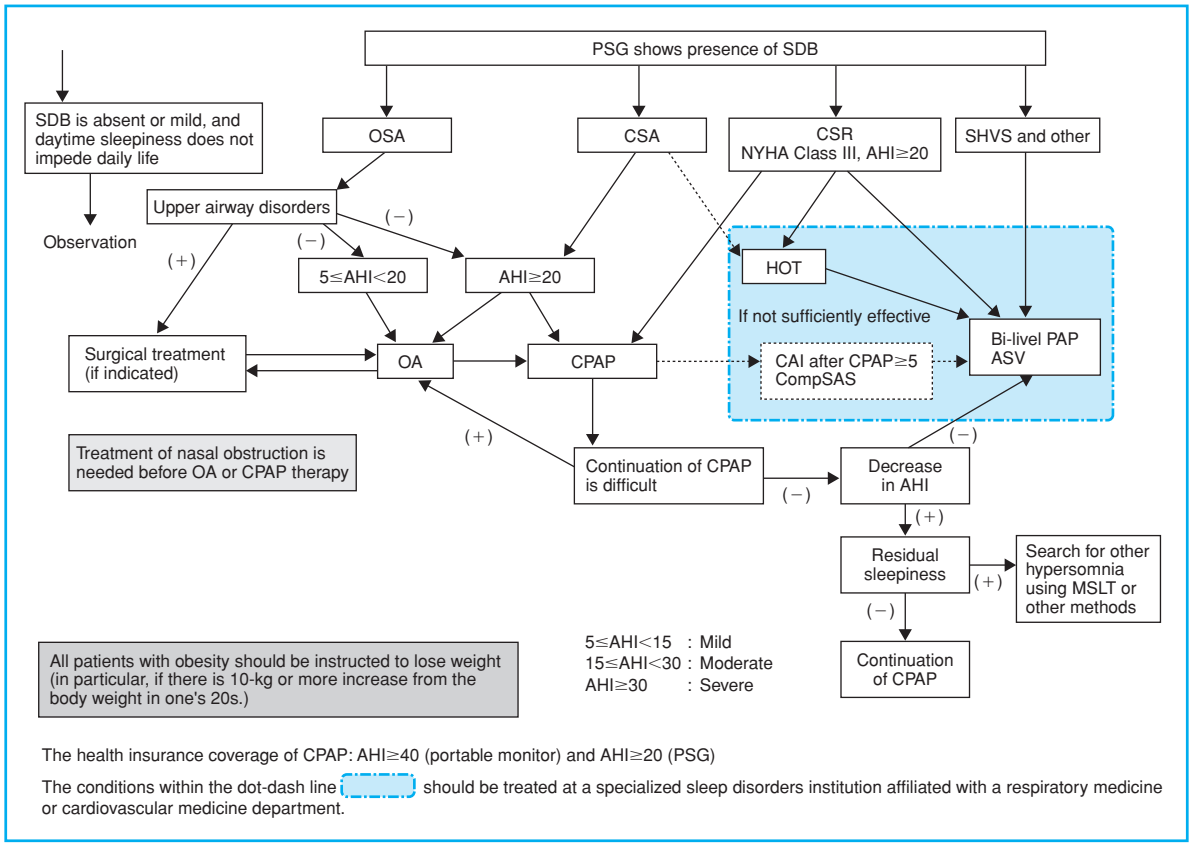


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Fig. 3 Treatment algorism for sleep-disordered breathing (SDB)

When introduction of HOT or ASV is required in the treatment of SDB accompanying heart failure, patients should be referred to specialized sleep disorders institutes affiliated with respiratory medicine or cardiology departments. When the SDB condition has stabilized through home therapy of continuous positive airway pressure (CPAP) therapy or other means, patients would be reverse-referred to general medical institutions. Because weight gain leads to aggravation of SDB, treatment plans at all medical institutions should include the management of lifestyle-related diseases, including obesity and metabolic syndrome.

Efficacy of CPAP Therapy

The first-line therapy for SAS is CPAP. The CPAP therapy has been used for more than a quarter of a century since it was first described by Sullivan et al. in 1981, and its effectiveness has been proven all over the world. In Japan, CPAP was covered by the health insurance system in 1998, and this therapy has since been used mainly in the practice of respiratory medicine. While OSAS is an independent risk factor of hypertension, CPAP therapy improves hypertension usually by about 10 mmHg.[2] In 2005, the 10-year followup study conducted by Marin et al.[14] in Spain demonstrated that severe OSAS patients had a significantly higher risk of developing nonfatal and fatal cardiovascular diseases than normal individuals, and the CPAP therapy significantly lowered the incidence rate of these diseases.

The use of CPAP to facilitate early diagnosis and appropriate treatment of OSAS and other

forms of SDB is clinically important not only as a means for primary prevention of obesity-related conditions called lifestyle-related diseases, but also as a factor affecting the life prognosis of cardiovascular diseases and stroke, the two leading causes of death. In addition, it also bears a social importance because of its potential effectiveness in preventing drowsiness-related accidents and injuries.

Post-CPAP Therapy

As the CPAP therapy for SAS has come into widespread use in various clinical departments, much discussion has arisen as to what would be the best therapy to choose after CPAP (post-CPAP therapy). The most representative post-CPAP therapy is the oral appliance (OA) therapy, which was brought under the coverage of the national health insurance system in dentistry in 2004.[10] Notable surgical therapies include minimally invasive operations such as radio-frequency therapy and soft palate implant operation in otolaryngology, as well as maxillomandibular advancement surgery and orthognathic surgery in oral surgery. Drug therapy (modafinil) for residual sleepiness after CPAP is also promising.

In the field of cardiovascular medicine, HOT for CHF has became available within the health insurance system. On the other hand, the CANPAP study[15] in Canada reported the limitations of CPAP therapy for CHF accompanying CSAS, and a study in 2007 demonstrated the effectiveness of ASV against complex SAS (CompSAS), which is characterized by increased central sleep apnea after CPAP therapy.[16] There are many developments taking place in this field.

Expanding Roles of SAS Care

The complex manifestations of SAS such as hypoxemia, acidosis, and exaggerated negative intrathoracic pressure may be the underlying factors of various diseases that develop or aggravate during sleep at night or in the early morning, but little attention has been paid to the involvement of such factors.

Recently, associations were demonstrated between SAS and nocturnal sudden death and between SAS and stroke.[17,18] SAS is also associated with gastroesophageal reflux (GER) and non-alcoholic steatohepatitis (NASH) in the field of gastroenterology, as well as nocturia and erectile dysfunction (ED) in the field of urology. In industrial medicine, SAS is involved in the causation of drowsiness-related accidents, and much attention is directed to SAS treatment as a potential means of accident prevention (Fig. 1). In obstetrics (perinatal medicine), in relation to the adverse fetal effect of serious hypoxemia resulting from severe SAS in obese pregnant women, a possibility has been suggested that the treatment of SAS using CPAP may improve pregnancy-induced hypertension, reduce miscarriages and premature births, and protect the lives and brain function of fetuses.[19]

Conclusion

The diagnosis and treatment of SDB, with particular focus on SAS, should be expanded further among general clinicians. As stated in the Guidelines for Diagnosis, Treatment, and Clinical Collaboration in SDB,[5] an essential prerequisite for the diagnosis and treatment of SDB is the establishment of sleep disorders institutions serving key functions. On this basis, we need to develop collaboration among internal medicine, otolaryngology, psychiatry, and dentistry/oral surgery departments (inter-department collaboration). In the future, we need to promote further verification of the guidelines based on the accumulation of evidence and the phased construction of comprehensive SDB care systems and networks including regional medical collaboration.

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List of Main Abbreviations

AHI; apnea hypopnea index
ASV; adaptive pressure support servo-ventilation
CAI; central apnea index
CompSAS; complex sleep apnea syndrome
CPAP; continuous positive airway pressure
CSA; central sleep apnea
CSAS; central sleep apnea syndrome
CSR; Cheyne-Stokes respiration
EDS; excessive daytime sleepiness
ESS; Epworth sleepiness scale
HOT; home oxygen therapy
MSLT; multiple sleep latency test
NYHA; New York Heart Association
OA; oral appliance
ODI; oxygen desaturation index
OSA; obstructive sleep apnea
OSAS; obstructive sleep apnea syndrome
PAP; positive airway pressure
PLMS; periodic limb movements during sleep
PSG; polysomnography
RBD; REM sleep behavior disorder
RWA; REM sleep without atonia
SAS; sleep apnea syndrome
SDB; sleep-disordered breathing
SHVS; sleep hypoventilation syndrome
SOREMP; sleep onset REM period
SpO_2; arterial oxygen saturation by pulse oximetry