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Work report by the task force of the Japanese Academy of Dental Sleep Medicine for clinical practice guidelines of oral appliances

OKUNO Kentaro[1)], SATO Kazumichi[2)], ARISAKA Takehiro[3)], GOTOH Motohiro[4)]
SASAO Yasuhiro[5)], TAGA Hitoshi[6)], HAMADA Suguru[7)], HOSOHAMA Kyoko[8)]
YAMAMOTO Tomoyoshi[9)], IRIE Michinori[10)], KASHIWAZAKI Jun[11)], KADOTANI Hiroshi[12)]
SATO Mitsuo[13)], SUZUKI Masaaki[14)], HIGURASHI Naoki[15)], SAKAKIBARA Hiroki[16)]
SHIMIZU Tetsuo[17)], SUGISAKI Masashi[18)], TONOGI Morio[19)]

日本睡眠歯科学会口腔内装置診療ガイドライン作成委員会の活動報告

奥野健太郎[1)]，佐藤一道[2)]，有坂岳大[3)]，後藤基宏[4)]
佐々生康宏[5)]，田賀　仁[6)]，濱田　傑[7)]，細濱教子[8)]
山本知由[9)]，入江道文[10)]，柏崎　潤[11)]，角谷　寛[12)]
佐藤光生[13)]，鈴木雅明[14)]，日暮尚樹[15)]，榊原博樹[16)]
清水徹男[17)]，杉崎正志[18)]，外木守雄[19)]

Abbreviations list

OSA = obstructive sleep apnea; OA = oral appliance; CPAP = continuous positive airway pressure; GRADE = Grading of Recommendations Assessment Development and Evaluation, JADSM = The Japanese Academy of Dental Sleep Medicine, PSG = polysomnography; RCT = randomized controlled trial; AHI = apnea hypopnea index; ESS = Epworth Sleepiness Scale; QOL = quality of life

[1)] Division of Functional Oral Neuroscience, Osaka University Graduate school of Dentistry（大阪大学大学院歯学研究科顎口腔機能治療学教室）
[2)] Department of Oral Medicine, Oral and Maxillofacial Surgery, Tokyo Dental College（東京歯科大学オーラルメディシン・口腔外科学講座）
[3)] Ota Memorial Sleep Center, Sleep Surgery Center（太田総合病院睡眠科学センター睡眠外科学センター）
[4)] Second Department of Oral and Maxillofacial Surgery, Osaka Dental University（大阪歯科大学口腔外科学第二講座）
[5)] Center for Oral Functional Disorders, Sasao Dental Clinic（ささお歯科クリニック口腔機能センター）
[6)] Dentistry & Oral Surgery, JR Tokyo General Hospital（JR東京総合病院歯科口腔外科）
[7)] Department of Oral and Maxillofacial Surgery, Kinki University Faculty of Medicine（近畿大学医学部歯科口腔外科学教室）
[8)] Department of Oral Medicine, Oral and Maxillofacial Surgery, Tokyo Dental College（東京歯科大学オーラルメディシン・口腔外科学講座）
[9)] Department of Oral and Maxillofacial Surgery, Yokkaichi Municipal Hospital（市立四日市病院歯科口腔外科）
[10)] Irie Clinic, Orthodontic Office（矯正歯科入江クリニック）
[11)] Asahigaoka Jun Dental Clinic（旭ヶ丘ジュン歯科）
[12)] Department of Psychiatry, Shiga University of Medical Science（国立大学法人滋賀医科大学医学部附属病院精神科）
[13)] Educational System in Dentistry, Graduate School, Tokyo Medical and Dental University（東京医科歯科大学大学院医歯学総合研究科歯学教育システム評価学分野）
[14)] Department of Otolaryngology, Teikyo University Chiba Medical Center（帝京大学ちば総合医療センター耳鼻咽喉科）
[15)] Cosmos Dental Clinic, Mabashi Clinic（コスモス歯科馬橋クリニック）
[16)] Tokushige Kokyuki Clinic（とくしげ呼吸器クリニック）
[17)] Department of Neuropsychiatry Section of Neuro and Locomotor Science, Akita University School of Medicine（秋田大学精神科学講座）
[18)] Department of Dentistry, Jikei University School of Medicine（東京慈恵会医科大学歯科学教室）
[19)] Department of Oral and Maxillofacial Surgery, Nihon University School of Dentistry（日本大学歯学部口腔外科学教室第1講座）

Oral appliance therapy was approved by national health insurance in Japan in 2004 and oral appliances (OAs) have since been widely used in the treatment of obstructive sleep apnea (OSA). We herein described the process of making clinical practice guidelines by the task force of the Japanese Academy of Dental Sleep Medicine as a work report. In Japan, OAs are covered by national health insurance. In consideration of the balance between medical treatment fees and the price of technical materials, we used a single-piece (monoblock) OA that advanced the mandible forward and limited mouth opening in OSA patients in Japan. The Japanese Academy of Dental Sleep Medicine (JADSM) focused on OAs frequently used for the treatment of OSA in Japan, and considered an evaluation of their effects to be necessary.

Clinical practice guidelines were developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system.

We recommend OAs that advanced the mandible forward and limited mouth opening for patients with OSA. However, CPAP should be used by patients for whom it has been indicated. OAs are desirable for those who cannot use CPAP (GRADE 1B, strong recommendation/quality of evidence, "Moderate quality").

The long-term effects and side effects, OSA severity, and comorbidities of OA therapy were not examined, which represented a limitation to the present study. In future studies, the Japanese Academy of Dental Sleep Medicine plan to update clinical practice guidelines for oral appliances used in OSA.

Key words: obstructive sleep apnea (OSA), oral appliance (OA), continuous positive airway pressure (CPAP), Grading of Recommendations Assessment Development and Evaluation (GRADE), clinical practice guidelines
(閉塞性睡眠時無呼吸症候群, 口腔内装置, 経鼻的持続陽圧呼吸療法, GRADE, 診療ガイドライン)

1.0 Introduction

An oral appliance (OA) is a device that fits within the oral cavity and prevents upper airway collapse in patients with OSA. The American Academy of Sleep Medicine (AASM) guidelines recently concluded that OAs were less effective than continuous positive airway pressure (CPAP) and recommended OAs as an alternative to CPAP to treat mild to moderate OSA and severe OSA when CPAP was refused or not tolerated[1].

A systematic review[2] and the Cochrane review[3] on the effects of OA reported increasing evidence to suggest that subjective sleepiness and sleep-disordered breathing were ameliorated by OAs relative to those in a control, and also that CPAP appeared to be more effective in improving sleep study measures, including AHI, lowest SpO_2, and arousal index than an OA. However, many different OA devices are available for OSA, such as those that advance the mandible forward or suction the tongue forward, and also single-piece (monoblock) and two-piece (duoblock) appliances.

In Japan, OAs are covered by national health insurance. In consideration of the balance between medical treatment fees and the price of technical materials, we used a single-piece (monoblock) OA that advanced the mandible forward and limited mouth opening in OSA patients in Japan. The Japanese Academy of Dental Sleep Medicine (JADSM) focused on OAs frequently used for the treatment of OSA in Japan, and considered an evaluation of their effects to be necessary. We have reported the clinical practice guideline in Journal of Oral and Sleep Medicine[4]. We herein described the process of making clinical practice guidelines by the task force of the Japanese Academy of Dental Sleep Medicine as a work report.

2.0 The process involved in making clinical practice guidelines

The JADSM Board of Directors approved the development of clinical practice guidelines for oral appliance therapies in patients with obstructive sleep apnea in October 2011, and approved the appointments of Task Force members in December 2011.

The purpose of these clinical practice guidelines was to provide information to dental and medical doctors engaged in sleep medicine. We performed this meta-analysis and developed these clinical practice guidelines using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system (**Figure 1**)[5-7]. **Figure 2** and **Table 1** show the process used to make these clinical

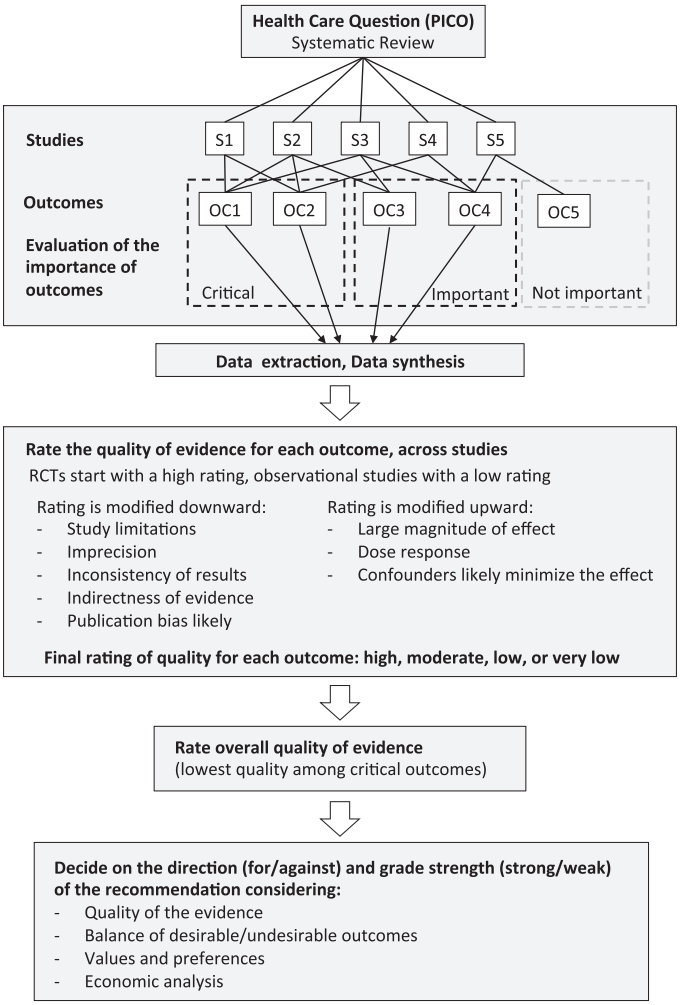

Figure 1 Schematic view of GRADE's process for developing recommendations
RCTs: randomized controlled trials. Adopted from [7].

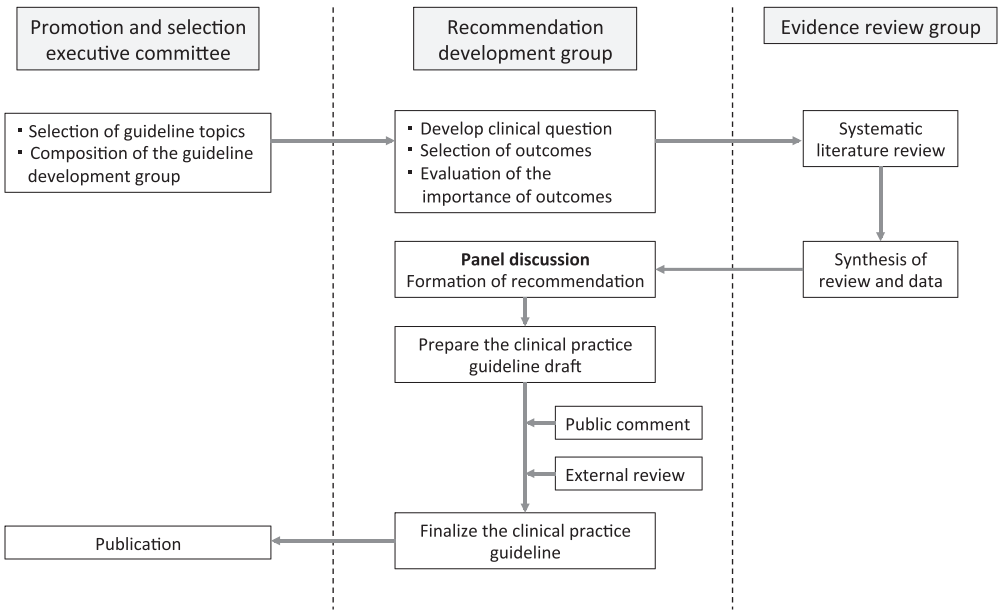

Figure 2 The role of each group in process for developing clinical practice guidelines
Adopted from [8].

Table 1 The process involved in making clinical guidelines

Date	Contents
December, 23, 2011	Clinical Questions, Outcome Selection, & Importance
April, 16, 2012	Literature Search
September, 22, 2012	Rating of The Quality of Evidence & Meta-analysis
September, 23, 2012	Adverse Events, Value and Preference, Economic analysis
December, 16, 2012	Panel Discussion
April, 8-26, 2013	Offering Public Comment to JADSM
July, 14, 2013	AGREE II Assessment by Two Outsider Reviewers
September, 16, 2013	Public Release to the Home Page (http://jadsm.jp/iryo/guideline_pdf/guideline_2013.pdf)

JADSM = The Japanese Academy of Dental Sleep Medicine; AGREE Ⅱ = Advancing the science of practice guidelines Ⅱ

practice guidelines[8].

2.1 Clinical Question

The aim of these guidelines by the Japanese Academy of Dental Sleep Medicine is to explore the following clinical question; Are OAs effective for patients with obstructive sleep apnea. To develop this clinical question, we used patient questions as a reference.

2.2 Selection of Outcomes and Evaluation of the Importance of Outcomes

We selected the following outcome measures: severity of sleep-disordered breathing (as measured by the Apnea Hypopnea Index (AHI), lowest SpO_2, and the arousal index in polysomnography), subjective daytime sleepiness (as measured by the Epworth Sleepiness Scale (ESS)), sleep-related quality of life (as measured by General Health, Mental Health, Vitality components of the SF-36 Health Survey), cardiovascular events, and mortality.

We evaluated the importance of outcomes according to three grades: critical, important but not critical, and not important. We considered AHI, ESS, Arousal, and QOL to be "critical" and SpO_2 to be "critical", as previously reported[4].

2.3 Literature Search

This study searched the following databases from the earliest records to 16 April 2012: MEDLINE, Cochrane Central Register of Controlled Trials, and Japan Medical Abstracts Society. The systematic literature search returned 102 articles. After applying the exclusion criteria, three authors agreed that 5 studies remained eligible and the full articles were retrieved. The method of the literature search have been reported in a systematic review article[9].

2.4 Synthesis of Review and Data

The GRADE approach[6] was used to evaluate the overall quality of evidence using an adapted version of the criteria advocated by the Cochrane Back Review Group[10]. In brief, the GRADE classification was downgrade by 1 level for each of the 5 factors considered: study limitations, inconsistency, indirectness, imprecision, and publication bias. We judged whether the 5 factors were present for each outcome. A GRADE profile was completed for each pooled estimate. The following definitions of the quality of evidence were applied[5]: High quality (further research is very unlikely to change our confidence in the estimate of the effect), moderate quality (further research is likely to have an important effect on our confidence in the estimate of the effect and may change the estimate), low quality (further research is very likely to have an important effect and is likely to change the estimate), and very low quality (we are very uncertain about the estimate). The results of the assessment for the quality of evidence and meta-analysis used by the GRADE system for these guidelines have been reported in a systematic review article[9].

2.5 Adverse Events, Values and Preferences, and Economic Analysis

We analyzed adverse events, and values and preferences, and economic analysis about OA therapy as a conference documents for a panel discussion. The results of the assessment have been reported in a clinical practice guideline[4].

2.6 Panel Discussion

The GRADE methodology differs from other systems in

Figure 3 Panel discussion
Fifteen panel members voted based on data on the quality of evidence, a balance between benefits and adverse events, values, and preferences.

that it makes guideline recommendations relatively simple and transparent. Only two possible recommendations can be made as follows: (1) strong or (2) weak/conditional. A strong recommendation means that most patients should receive the recommended course of medical care. A weak/conditional recommendation means that, although most patients would select the recommended action, there are different choices that will be appropriate for different patients depending on their particular situation.

The panel discussion was held on December 16 2012 (**Figure 3**). Fifteen panel members consisting of three medical doctors, six dental doctors, one nurse, one dental hygienist and three healthcare customers voted based on data on the quality of evidence, a balance between benefits and adverse events, values, and preferences.

The following recommendation[4] was ultimately adopted in the panel discussion.

"We recommend the use of OAs that advanced the mandible forward and limited mouth opening for patients with OSA. However, CPAP should be used by patients for whom it has been indicated. OAs are desirable for those who cannot use CPAP (GRADE 1B, strong recommendation/quality of evidence, "Moderate quality").

Remarks

The usefulness of OAs was confirmed in this study. However, this study does not recommend a change in treatment principles to OA therapy when CPAP cannot be used by patients. When CPAP cannot be used, its cause should be identified, and measures to exclude these causes (nasal disease, inappropriate pressure, unfit mask, and poor management) should be evaluated.

The results of the vote on the use of OAs for patients with OSA showed that strong for use was 13, weak for use was 1, weak for not using was 0, and strong for not using was 0.

3.0 Discussion

The long-term effects and side effects, OSA severity, and comorbidities of OA therapy were not examined, which represents a limitation of the present study. Although observational studies investigated the long-term effects[11] and side effects[12, 13], OSA severity[14], and comorbidities[15] of OA therapy, we could not in the present study because there were no RCT. In order to consider the long-term efficacy of OA, observational studies need to be included in the selection criteria of the study design. The selection of RCT only represented another limitation of this study.

The findings are limited by the relatively small number of patient studies and methodological weaknesses, such as the lack of blinding. The blinding of patients or assessors was impossible because the device shape completely differed between OA and CPAP therapies. Thus, blinding was absent in this study, which decreased the evidence grade.

Although co-operation was required between a large number of individuals in the clinical practice guidelines task force, dental and medical doctors, health-care workers, and medical consumers, their lack of understanding about clinical practice guidelines sometimes led to difficulties. Therefore, the understanding of clinical practice guidelines themselves may be the most important for developing them. The JADSM held seminars to facilitate understanding the clinical practice guidelines and sharing the information about GRADE system on February 26th, July 3rd, October 15th 2011. We believe that this working report may help dental and medical doctors, health-care workers, and medical consumers to understand these clinical practice guidelines. This is posted as an example of the guideline that have optimally applied the GRADE framework (http://www.gradeworkinggroup.org/guidelines/index.htm).

In future studies, the Japanese Academy of Dental Sleep Medicine plan to update clinical practice guidelines for oral appliances used in OSA and support understanding of the clinical practice guidelines.

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Dr. Makoto Kikuchi served as chairman of the clinical practice guidelines for oral appliances task force and played a major role in this guideline. However, he has gone on March 27, 2014.

Dr. Noboru Emori played a major role in recommendation development group. However, he has gone on December, 2012. We appreciate Dr. Makoto Kikuchi and Dr. Noboru Emori, and commemorate their death. The Japanese Academy of Dental Sleep Medicine will memorize their achievement for all eternity.

Conflict of interests

The authors indicated no potential conflict of interests.

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