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Quality of life after adenotonsillectomy for children with sleep-disordered breathing: A linear mixed model analysis☆

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A B S T R A C T

Objective: To study changes in quality of life (QoL) after adenotonsillectomy (T&A) in children with sleep-disordered breathing (SDB), and to elucidate discrepancies in QoL improvements after T&A in children of different gender, age, adiposity status, and disease severity.

Materials and methods: Children aged 2–18 years were recruited. All children had SDB-related symptoms and underwent preoperative full-night polysomnography (PSG). Caregivers completed the first obstructive sleep apnea 18-items questionnaire (OSA-18) prior to T&A and the second OSA-18 survey within 3 months after surgery. Disease severity was defined as primary snoring (apnea/hypopnea index, AHI < 1), mild obstructive sleep apnea (OSA) ($5 > \text{AHI} \geq 1$), and moderate-to-severe OSA ($\text{AHI} \geq 5$). Discrepancies in OSA-18 score changes after T&A for different groups were assessed using the linear mixed model.

Results: In total, 144 children were enrolled (mean age, 7.0 ± 3.6 years; 76% boy). The OSA-18 total score changes after surgery were not significantly different by gender (boys *vs.* girls), age group (≥6 years *vs.* <6 years), or adiposity (obese *vs.* non-obese). The OSA-18 total score changes after surgery differed by disease severity (primary snoring *vs.* moderate-to-severe OSA, $P = 0.004$; mild OSA *vs.* moderate-to-severe OSA, $P = 0.003$). Children with moderate-to-severe OSA had greater improvement in OSA-18 total score after surgery than those with mild OSA or primary snoring.

Conclusions: Children with SDB had QoL improvement after T&A, as documented by OSA-18 score changes. The QoL improvement after T&A for SDB children increased as disease severity increased, and the improvement was not affected by gender, age, or adiposity.

1. Introduction

Sleep-disordered breathing (SDB) includes a spectrum of upper airway disorders ranging from primary snoring to obstructive sleep apnea (OSA) [1,2]. The prevalence of habitual snoring in children is 9–10%, while that of OSA is 1–3% [3,4]. Notably, SDB in children is due primary to enlarged tonsils and adenoids that obstruct the upper airway [1,2,5]. Removing tonsils and adenoids (adenotonsillectomy, T&A) is considered worldwide the first-line therapy for pediatric SDB [6–10].

Full night polysomnography (PSG) is the gold standard for diagnosing SDB in children [2]. Mounting evidence shows that PSG parameters improved dramatically after T&A [6–10]. Furthermore, for children with SDB, T&A improved outcomes in sleep studies, and positively influenced quality of life (QoL) [11,12]. Among available QoL instruments, the obstructive sleep apnea 18-items quality of life questionnaire (OSA-18) is a widely used disease-specific QoL survey for pediatric obstructive sleep disorders [13]. According to literature, children had significant short-term and

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long-term QoL improvements after T&A, as documented by changes in OSA-18 scores [12,14–16]. However, factors affecting QoL changes after T&A for children with SDB, have not been verified.

This study elucidates changes in QoL for children with SDB underwent T&A. In particular, this study investigates discrepancies in QoL changes after T&A for children of different gender, age, adiposity status and disease severity.

2. Materials and methods

2.1. Study population

The study protocol and informed consent for OSA-18 questionnaires were approved by the Ethics Committee of the National Taiwan University Hospital. From July 2010 to December 2012, children aged 2–18 years were recruited. Children were enrolled when they had signs and symptoms of a sleep disturbance including snoring, mouth breathing, and witnessed breath holding by caregivers for at least 1 month duration [17]. Adenoid size was determined using a lateral cephalometric radiograph. The adenoidal–nasopharyngeal (AN) ratio was measured on the lateral radiograph as the ratio of adenoidal depth to nasopharyngeal diameter according to the method by Fujioka et al. [18]. Tonsils were graded using the scheme by Brodsky et al. [19]: grade I, small tonsils confined to the tonsillar pillars; grade II, tonsils extending just outside the pillars; grade III, tonsils extending outside the pillars, but do not meet at the midline; grade IV, large tonsils that meet at the midline. Children with an AN ratio $\geq$0.5 or tonsil grade $\geq$2 underwent T&A as definite treatment. Exclusion criteria were (1) prior tonsil, adenoid, or pharyngeal surgery; (2) cranio-facial anomalies; (3) genetic disorders, neuro-muscular diseases, or mental retardation.

Basic data, clinical history, physical examination data were obtained. The weight and height of each child were measured, and the age- and gender-corrected body mass index (BMI) was applied for each child using established guidelines [20]. Obesity was defined as a BMI higher than the 95th percentile for a child's age and gender [5,9,20,21]. All subjects underwent a preoperative PSG study to define SDB severity [22]. The QoL assessment tool is based on the OSA-18 questionnaire, which is an 18-item questionnaire completed by the subject's caregiver [13,23].

2.2. Polysomnography (PSG)

All subjects completed an overnight PSG study before and after surgery. The overnight PSG (Embla N7000, Medcare Flaga, Reykjavik, Iceland) was performed in the sleep lab following a protocol described elsewhere [5,9,19,23,24]. The sleep stage and respiratory events were scored based on the 2007 American Academy of Sleep Medicine standard [22]. Obstructive apnea was defined as the presence of continued inspiratory effort associated with a >90% decrease in airflow for duration of $\geq$2 breaths. Hypopnea was defined as a $\geq$50% decrease in airflow for duration of $\geq$2 breaths that was associated with arousal, awakening, or reduced arterial oxygen saturation of $\geq$3%. Disease severity was defined as primary snoring (apnea/hypopnea index, AHI <1), mild obstructive sleep apnea (OSA) ($5 > \text{AHI} \geq 1$), and moderate-to-severe OSA ($\text{AHI} \geq 5$) [6–9].

2.3. OSA-18 QoL questionnaire (OSA-18)

All subjects completed the validated OSA-18 questionnaires before and after surgery. Franco et al. [13] first designed the OSA-18, and Kang et al. [23] translated and validated the traditional Chinese version. As a caregiver-administered QoL survey, the OSA-18 contains 18 items divided into five subscales: sleep disturbance; physical symptoms; emotional distress; day-time function; and caregiver concerns. Each is scored on a 7 point ordinal scale. The OSA-18 is graded to produce a score for each item, additional scores for the 5 sub-scales, and a total score. The OSA-18 total score is the sum of scores for the 18 items and, therefore, ranged from 18 (no impact on QoL) to 126 (major negative impact) [13,23].

2.4. Adenotonsillectomy (T&A)

Tonsillectomy was performed using the coblation method, and adenoidectomy was performed using the microdebrider-assisted method. All surgical procedures were performed in a single stage under general anesthesia, followed by hospitalization for two days [9,25].

2.5. Statistical analysis

Data were analyzed using SPSS Statistics 20.0 (IBM Corporation, New York, United States). Continuous data were expressed as the mean and standard deviation, and categorical data as the number and percentage. Continuous data before and after surgery were compared using the paired-sample *t*-test. The standard response mean (SRM), defined as the difference score divided by its standard deviation, was applied to estimate the strength of improvement in OSA-18 scores. The SRM of effect size increased with improvements in life quality among children who underwent T&A [26].

The main objective of this study is to explore whether the improvement of QoL before and after T&A differs between different subgroups. The use of linear mixed models (LMM) for analyzing repeated-measure data results in a more precise parameter estimation than that in traditional statistical methods (*e.g.*, linear regression) [27–30]. The equation of LMM consists of two levels.

Equation in level 1

$$Y_{ij} = \pi_{0i} + \pi_{1i}\text{TIME}_{ij} + e_{ij}$$

Equation in level 2

$$\pi_{0i} = \beta_{00} + \beta_{01}\text{Gender}+\beta_{02}\text{Age}+\beta_{03}\text{Adiposity} + \beta_{04}\text{Severity} + r_{0i}$$

$$\pi_{1i} = \beta_{10} + \beta_{11}\text{Gender}+\beta_{12}\text{Age} + \beta_{13}\text{Adiposity} + \beta_{14}\text{Severity} + r_{1i}$$

Note: Y_{ij} denotes individual *i*s OSA-18 score at time *j* where $j = 0$ or 1 represents pre-surgery and post-surgery, respectively.

In level 1, only time-varying covariate (TIME) is included and it indicates each individual's growth trajectory of outcome measure (π_{1i}) by releasing its random effect in level 2 (r_{1i}). On the other hand, each individual's response at baseline (π_{0i}) is allowed to differ by releasing its random effect in level 2 (r_{0i}). In level 2, the regression coefficients (β_{01}–β_{04}) represents that each participants' initial status (intercept) will be associated with their covariates. Importantly, the regression coefficients (β_{11}–β_{14}) indicates the interaction terms of time by the covariates which represents that the impact of time (π_{1i}) on outcome will be associated with their covariates. That is, the changes in OSA-18 score (time effect) are significantly different for a given subgroup when a significant interaction term appears.

As listed in the above equations, we adjusted for fixed effects for time, gender, age, adiposity, disease severity, and two-way interaction terms of time by each covariate as well as random effects for the intercept (baseline score) and time effect (linear slope). The random effect for the intercept was estimated, indicating that the baseline score changed across subjects. The