Cardiac Remodeling and Dysfunction in Children with Obstructive Sleep Apnoea – A Community Based Study

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ABSTRACT

Background: Childhood obstructive sleep apnoea (OSA) is suggested to be associated with cardiac structural abnormalities and dysfunction but existing evidence are limited and the treatment effect on echocardiographic outcome remains controversial.

Objective: To examine for the presence of subclinical cardiac abnormalities in childhood OSA and the effects of treatment on cardiac changes.

Methods: Polysomnography (PSG) and echocardiographic examinations were performed on 101 children aged between 6 and 13 years were invited from a community based questionnaire survey. They were classified into reference group (Apnoea-hypopnoea index (AHI)<1, n=35), mild OSA group (AHI 1-5, n=39) and moderate-to-severe group (AHI>5, n=27) based on PSG result. Treatments including adenotonsillectomy or nasal steroid were offered to the mild and moderate-to-severe OSA group.

Results: Moderate-to-severe OSA group had greater right ventricular (RV) systolic volume index (RVSVI), lower RV ejection fraction (RVEF) and higher RV myocardial performance index (RVMPI) than the reference group. They also had more significant left ventricular (LV) diastolic dysfunction and remodeling with larger interventricular septal thickness index (IVSI) and relative wall thickness than those with lower AHI values. Moderate-to-severe OSA group had an increased risk of abnormal LV geometry compared to reference group [OR(95%CI) = 4.21(1.35–13.12)]. Log-transformed AHI was associated with RVSVI (p=0.0002), RVEF (p=0.0001) and RVMPI (p<0.0001) independent of the effect of obesity. Improvement in RVMPI, IVSI, and E/e’ were observed in those with significant reduction in AHI (>50%) comparing 6 months to baseline.

Conclusions: OSA is an independent risk factor for subclinical RV and LV dysfunction, and improvement in AHI is associated with reversibility of these abnormalities.

Abstract word count: 257
INTRODUCTION

Childhood obstructive sleep apnoea (OSA) is being increasingly recognized and its prevalence among the paediatric population is reported as between 2-4%.1 Early studies on childhood OSA have demonstrated that severe disease can lead to congestive heart failure.2,3 More recent reports have documented the presence of subclinical forms of cardiac/ventricular dysfunction in children with OSA.4-7 However, these paediatric studies are limited by their small sample size and lack of normal children as controls. All cases included in these studies were recruited from hospital attendants, which may not truly reflect the situation in the community. Furthermore, the effect of intervention for OSA on cardiac dysfunction has not been well characterized. Preventing the development of subclinical cardiac abnormalities may be important as current evidence suggest asymptomatic ventricular dysfunction predicts future cardiovascular events.8,9 The aims of this study were to assess cardiac structure and function in an OSA cohort recruited from the community and to measure the degree of reversibility following interventions.

METHODS

Subjects and study design

Subjects for this study were drawn from our on-going childhood OSA epidemiological study, which involved children aged between 6 and 13 years recruited from thirteen randomly chosen schools. A total of 6447 school children had completed a validated OSA screening questionnaire10 that stratified them into high (n = 586) or low risk (n = 5861) for OSA. All children classified as high risk by the questionnaire were invited and subjects classified as low risk group were randomly chosen and invited for overnight polysomnography (PSG) and cardiac assessment. Four hundred and ten high risk and 209 low risk children agreed to participate. Children were excluded from the study if they had an intercurrent upper respiratory tract infection within 4 weeks of PSG, suffered from neuromuscular disorder, craniofacial anomalies, syndromic disorder, or if they had previously undergone upper airway surgery. Anthropometric parameters including weight, height, waist and hip circumferences and casual systolic and diastolic blood pressure (BP) were measured (Datascope Accutorr Plus) on the day of PSG. Two BP measurements were taken with a 5-min interval and the average of the two readings was used for analysis. Body mass index (BMI) was translated to BMI z score according to the normal reference values of Hong Kong Chinese children.11 This project included the first 101 consecutive children who gave consent for overnight PSG and echocardiographic examination (ECHO).

All children were referred for otorhinolaryngological assessment before their PSG. For those who were diagnosed to have OSA based on PSG, adenotonsillectomy would be offered. Those who
refused surgical intervention or surgery thought not to be indicated based on pre-determined criteria (small tonsils; tonsils not extend beyond the anterior tonsillar pillar and small adenoids; adenoids which occupy less than 25% of post-nasal space with minimal OSA symptoms or poorly controlled allergic rhinitis with supine nasal obstruction) were offered nasal corticosteroids therapy (mometasone 100 microgram per day for six months) and or non-invasive positive pressure ventilation (NIPPV). These subjects then underwent repeat PSG and ECHO 6 months after the operation or start of therapy. Children with OSA who refused any form of therapies were also invited to return at 6 months for repeat assessment. Informed consent from the parents or legal guardian and verbal assent from each child were obtained. The study was approved by the institutional ethical committee.

**Polysomnography**

Children recruited into the study underwent at least one standard overnight PSG at a dedicated sleep laboratory with CNS 1000P polygraph (CNS, Inc., Chanhassen MN). The central and occipital electroencephalogram, bilateral electrooculogram, submental electromyogram, bilateral leg electromyogram, and electrocardiogram were recorded. The positions of the subject, respiratory airflow (nasal cannula connected to pressure transducer), respiratory efforts (strain gauge), arterial oxyhaemoglobin saturation (SpO2, Ohmeda 3700 pulse oximeter, measured by finger sensor, averaging time = 3s) were measured. In this study, we scored the presence of both apnoeas and hypopnoeas. Briefly, obstructive apnoea was defined as absence of airflow with persistent respiratory effort lasting longer than two baseline breaths, irrespective of SpO2 changes. Obstructive hypopnoea was defined as reduction of airflow of 50% or more with persistent respiratory effort lasting longer than two baseline breaths and associated with oxygen desaturation of at least 4% and or arousals. Apnoea-hypopnoea index (AHI) was the total number of obstructive apnoeas or hypopnoeas per hour of sleep. Oxygen desaturation index (ODI) was defined as the total number of dips in arterial oxygen saturation ≥4% per hour of sleep. Arousal was defined as an abrupt shift in electroencephalogram frequency during sleep, which may include theta, alpha, and/or frequencies greater than 16Hz but not spindles, with 3-15 seconds in duration. In REM sleep, arousals were scored only when accompanied by concurrent increases in submental electromyogram amplitude. Arousal index (ArI) was defined as the number of arousal per hour of sleep. OSA was defined if AHI ≥1 per hour of sleep.

**Echocardiography (ECHO)**

ECHO studies were performed using the Vivid 5 system (Vingmed-General Electric, Horten, Norway). The examiner was blinded to the subject’s PSG result and therefore group allocation. LV volumes and ejection fraction (EF) were assessed by biplane Simpson's equation using the apical
four-chamber and two-chamber views, where the length of the ventricular image was maximized. LV mass was measured by the Devereux’s method as previously described.\(^\text{14}\) LV mass was divided by subject’s height to the power of 2.7 to provide LV mass index (LVMI). Left ventricular hypertrophy (LVH) was defined as an LVMI greater than 95th percentile of healthy control (38.6 g/m\(^2.7\)) that was previously reported.\(^\text{15}\) The relative wall thickness (RWT) of LV, a measure of concentricity, was calculated as the sum of the thickness of the posterior and septal wall divided by LV diastolic diameter. A RWT of greater than 95th percentile of age matched healthy control (0.375) that was previously reported was used as cutoff to define concentric LV geometry.\(^\text{16}\) LV geometry was classified as normal, concentric remodeling, eccentric hypertrophy, or concentric hypertrophy as described by Ganau et al.\(^\text{17}\) Right ventricular end-systolic (RVSVI) and end-diastolic volume index to height (RVDVI) and the right ventricular ejection fraction (RVEF) were calculated from apical four chambers views, using the area-length method (RV volume=3/8\(\pi\)\([\text{area}^2/\text{length}]\)). Any significant valvular lesion was assessed with haemodynamic assessment made. In children with tricuspid regurgitation (TR), spectral Doppler profile was used to estimate pulmonary artery systolic pressure from the sum of modified Bernoulli equation (velocity\(^2\times4\)) product and estimated right atrial pressure. Diastolic function was measured for both ventricles by measuring the ratio of the peak early diastolic (E) and peak atrial (A) velocity from pulse doppler data of tricuspid and mitral valve. Left and right ventricle myocardial performance index (MPI) of both ventricles were defined by the sum of isovolumic contraction and relaxation times divided by ejection time obtained from pulse Doppler data. Left ventricular filling pressure was approximated from the relationship of E/e’ where E is the pulse wave Doppler velocity of mitral valve and e’ was the pulse wave tissue Doppler velocity of septal annulus.

**Statistical Analysis**

All the parametric and non-parametric data were expressed as mean ± SD and median (IQR) respectively. Parametric and non-parametric data were compared using one-way analysis of variance (ANOVA) and Krustal-Wallis test respectively. For parametric data, Tukey or Games-Howell method was used for post-hoc pair-wise comparisons with adjustments made depending on the agreement of the assumption of variance. For non-parametric data, Mann-Whitney U tests with adjusted p-value (significant at \(p<0.016\)) were used for pair-wise comparisons. Chi-square tests were performed to investigate the difference in proportions between groups. Further chi-square tests with adjusted p-value (\(p < 0.016\)) were used for pairwise comparisons.

Multiple linear regression analyses were performed to assess the relationship between PSG variables and ECHO measures, while controlling for possible confounders. As some of the PSG data were skewed and contained zero values, these variables were log-transformed using special
formula (natural log \([x+0.1]\)).

Logistic regression analyses were performed to estimate the odds ratios (OR) for abnormal LV geometry for different severity of OSA compared to reference group, while adjusting for possible confounding factors.

For the follow-up study, subjects were divided into 2 groups for comparison. One group consisted of subjects who had improvement in their OSA as defined by >50% reduction in AHI from baseline to follow-up\(^{18}\). The other group consisted of subjects who had persistent or worsened OSA (<50% reduction in AHI). Wilcoxon Signed Ranks tests were used to examine the intra-group differences between baseline and follow-up. Mann-Whitney U tests were used to detect the between-group differences at baseline, at follow-up and the changes during the treatment period. All the analyses were performed using the SPSS version 13.0.

RESULTS
Study population
Children were divided into reference group (AHI < 1 and snoring for < 3 nights per week, \(n = 35\)), mild OSA group (AHI 1 to 5, \(n = 39\)), moderate-to-severe OSA group (AHI > 5, \(n = 27\)) (figure 1). The demographics, anthropometric and PSG data between groups were shown in table 1, and there were no significant differences in all demographic and anthropometric parameters except for BMI z score. Significant differences were found in AHI, ODI, ArI and SpO2 nadir between groups.

ECHO Findings of Cardiac Structure and Function
Right Ventricle
RVSVI, RVEF and RVMPI were all significantly different between the three groups. Reference group had significantly smaller RVSVI and higher EF than both the mild and moderate-to-severe OSA groups. For RVMPI, post hoc test showed that the moderate-to-severe group had a significantly greater value than the mild and reference groups (table 2). No significant TR was noted in any of the children.

Multiple linear regression analysis showed that log-transformed AHI and log-transformed ODI were significantly associated with RVSVI \((p = 0.0002)\), RVEF \((p = 0.0001)\) and RVMPI \((p <0.0001)\) after adjustment for age, gender and BMI z score (table 3).

Left Ventricle
The relative wall thickness (RWT) and the interventricular septal thickness index to height (IVSI) were significantly higher in the moderate-to-severe group when compared to the mild group (table
2). Similar trend was observed for LVMI although subgroups comparison showed no significant difference. The moderate-to-severe group also had a greater proportion of subjects having abnormal LV geometry when compared to the mild and reference groups. For diastolic function parameters, E/e’, a marker of LV filling pressure, increased with increasing severity of OSA.

Multiple linear regression analysis showed that log-transformed ODI were significantly associated with IVSI (p = 0.016) after adjustment for age, gender and BMI z score. The results also showed that the adjusted association between log-transformed AHI and E/e’ was nearly significant (p = 0.050) (table 3).

Multivariate logistic regression analyses were used to examine whether the severity of OSA was associated with the presence of abnormal LV geometry. The risk of abnormal LV geometry was 4.29 times (OR = 4.29 [95%CI: 1.43–12.81], p = 0.009) higher for moderate-to-severe group when compared to reference group before adjusting for any confounders. The OR was reduced but remained significant after adjustment for age, gender and BMI z score (OR = 4.21 [95%CI: 1.35–13.12], p = 0.013). Such an increased risk was not found in the mild OSA group.

**Treatment Effect**

Thirty out of sixty-six OSA subjects refused to have follow-up assessment. Of the remaining 36 OSA subjects, 8 of them had adenotonsillectomy and 9 of them received nasal steroid therapy. No children opted to receive NIPPV in our study. The remaining 19 subjects refused any kind of treatment but agreed to have follow-up assessment (recruitment details were described in figure 1). Their characteristics including anthropometrics, polysomnographics and ECHO parameters were not significantly different from those who did not return for reassessment. At follow-up, 17 had improved OSA as reflected by their AHI decrement ≥50% (improved OSA group). The remaining (n = 19) were classified as persistent OSA group.

Significant reductions in RVMPI, IVSI, and E/e’ from baseline to 6 months follow up were noted only in the improved OSA group (table 4). Changes in RWT and E/e’ from baseline were significantly different between the improved OSA group and the persistent OSA group (table 4). Furthermore, change in AHI was positively associated with changes in RVMPI (Spearman’s rho (r) = 0.448, p = 0.006), IVSI (r = 0.429, p = 0.009), RWT (r = 0.433, p = 0.008) and E/e’ (r = 0.502, p = 0.002) (figure 2). These changes in ECHO parameters were not significantly associated with change in BMI z score.
DISCUSSION

In this study we were able to document RV and LV dysfunction and remodeling in a cohort of community based children with OSA. The AHI was demonstrated to be a significant independent parameter associated with cardiac dysfunction. Following effective treatment for OSA, the cardiac abnormalities improved whereas in the group with persistent OSA, the abnormalities showed no improvement. These findings are important because children who are otherwise healthy have end organ involvement with RV and LV structural and functional abnormalities similar to those that have been associated in other diseases, such as hypertension. In adults, evidence supports that abnormalities detected in ECHO even in asymptomatic patients predict future cardiovascular events. Regression of these cardiac abnormalities with treatment is associated with decreased in cardiovascular morbidity including atrial fibrillation, heart failure and hospitalization.

There are disparate conclusions of previous studies on the effect of OSA on RV function and enlargement. Sanner et al has shown that OSA was independently associated with depressed RVEF by radionuclide ventriculography. In other studies RV dimensions and RV systolic function measured by ECHO were not shown to be significantly different between subgroups with varying OSA severity. A possible explanation for the discrepancy is that previous studies were on subjects with varying degree of obesity recruited from hospital attendants. Obesity is an important risk factor of OSA for adult and children, and it is well established that obesity and its metabolic complications are risk factors for cardiac abnormalities. Thus failing to control for obesity could have given conflicting results in the relationship between OSA and RV dysfunction. Our study showed RVSVI, RVEF and RVMPI worsen with OSA severity, and AHI independently correlated with these parameters, even after adjusting for age, gender and BMI z score. Cor pulmonale was consistently observed in previous study on severe OSA children. On the other hand, none of the children in our study has cor pulmonale. Nonetheless, our study provides evidence for the first time that subclinical RV dysfunction already exists in children with mild degree of OSA. Further evidence to support RV involvement in childhood OSA is that RVMPI significantly improved after intervention as shown in our study as well as that reported by Tal et al. Moreover, the change in RVMPI from baseline to follow-up was significantly associated with the change in AHI (figure 2).

After controlling for age, gender and BMI z score, children with moderate-to-severe OSA had a 4.2-fold increased risk for abnormal LV geometry, when compared to reference group. This finding has important clinical implication as previous studies have found that in individuals with similar LV mass, altered LV geometry was associated with greater cardiovascular risk. Altered LV diastolic filling is expected from concentric hypertrophy, but there was no difference in mitral valve E/A between groups. The result may be accounted for by the sensitivity of early transmitral velocity (E)
to loading condition, heart rate, as well as increase LV mass. Transmural flow in relation to tissue
diastolic velocity Ea may be a better method in assessing diastolic function and E/e' was indeed
shown to increase with OSA severity. This is in agreement with another study on left ventricular
function in children with OSA where the authors also demonstrated a dose-dependent decrease in
diastolic function with increased OSA severity. Adenotonsillectomy in children with OSA has been
shown to improve growth, neurocognitive function, and nocturnal enuresis. Well conducted
studies that reported on the outcome of OSA treatment on cardiac findings are scarce. Görür et al
showed improvement in RV dimension, LV end diastolic diameter, and IVS assessed by ECHO
after adenotonsillectomy. Unique to our study is the presence of a persistent OSA group that
consisted of subjects who refused any treatment or did not have significant improvement after
treatment. All children received adenotonsillectomy had ≥50% reduction in AHI suggesting that
adenotonsillectomy is indeed an effective treatment of childhood OSA (figure 1). On the other hand
only 4 out of 9 children received nasal steroid therapy had ≥50% reduction in AHI. Significant
improvements in RVMPI, IVSI, and E/e' comparing 6 months to baseline were seen only in the
improved OSA group, and indeed the change in RVMPI and E/e' was associated with change in
AHI. In the mild OSA group 5 out of 18 untreated children had significant improvement in AHI
suggesting that some mild OSA cases may spontaneously improve with time. There may be a
practical need for follow up PSG for assessment of treatment efficacy and monitor progress of those
who do not receive treatment.

The severity of OSA in our sample population was milder than other studies as they were recruited
from the community. The results generated from our study are however, important as abnormal
cardiac function and structure could already be demonstrated in this community based cohort,
emphasizing the need to recognize OSA early in its progression. A proportion of OSA children did
not return for repeat assessment at 6 months, which is one of our limitations and a common
difficulty faced by paediatric researchers. On further analysis, there were no significant
differences in anthropometric, PSG and ECHO measurements between those who did not return and
untreated subjects. The cases with persistent OSA at follow-up had less severe disease at baseline
than the improved OSA group which may be a potential bias. As treatment was not randomised,
naturally parents of children with more severe OSA were more likely to opt for treatment and
especially surgery. Though milder disease at baseline, ECHO parameters of the persistent OSA
group did not improve with time. In contrast, significant improvements were seen following
treatment in the improved OSA group, signifying genuine beneficial effects of intervention. The
clinical significance of cardiac structural and functional changes described in this study, despite
being shown in adult studies to predict future clinical events, is not certain in children, and
will require longer follow up to better delineate their implications.
CONCLUSIONS
Childhood OSA is associated with RV and LV remodeling and dysfunction. Community based screening program may allow early detection and treatment of OSA that could potentially reverse myocardial dysfunction, remodeling and lessen the risk for future cardiovascular disease.
ACKNOWLEDGEMENTS
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COMPETING INTERESTS
The authors do not have any competing interests.

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REFERENCES


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Figure 1.

- **Consented for PSG & ECHO** (n = 101)
  - **Control**
    - AHI <1
    - snore <3 nights per week
    - (n = 35)
    - Refused follow-up
      - (n = 20)
  - **Mild OSA**
    - AHI between 1 and 5
    - (n = 39)
    - Follow-up
      - (n = 19)
    - Post Nasal Steroid
      - (n = 1)
    - Untreated
      - (n = 18)
    - OSA improved (AHI decreased by >50%)
      - n = 1
    - Untreated
      - n = 5
  - **Moderate-to-severe OSA**
    - AHI >5
    - (n = 27)
    - Refused follow-up
      - (n = 10)
  - **Follow-up**
    - (n = 17)
    - Post Surgery
      - (n = 8)
    - Post Nasal Steroid
      - (n = 8)
    - Untreated
      - (n = 1)
    - n = 8
    - n = 3
Figure 2.
Figure Legends

Figure 1. Flow Diagram
101 subjects consented to undergo polysomnography (PSG) and echocardiography (ECHO), of which 35 were controls, 39 had mild OSA and 27 had moderate-to-severe OSA. Twenty of the mild-OSA group and 10 of the moderate-to-severe-OSA group refused follow-up. The remaining were either treated with adenotonsillectomy or nasal steroid therapy, or left untreated because they refused any treatment. At follow-up, 17 of them had their AHI decreased by more than 50%.

Figure 2. Association between change in AHI and changes in ECHO parameters
The change in apnoea-hypopnoea index (ΔAHI) was significantly associated with the changes in (a) right ventricular myocardial performance index (ΔRVMPI), (b) interventricular septal thickness index (ΔIVSI), (c) relative wall thickness (ΔRWT) and (d) ratio of mitral early peak velocity/ mitral annulus early peak velocity (ΔE/e’).
**Table 1.** Demographic, anthropometric and PSG characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Total (N = 101)</th>
<th>Reference (N = 35)</th>
<th>Mild OSA (N = 39)</th>
<th>Moderate-to-severe OSA (N = 27)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics and Anthropometrics</strong></td>
<td></td>
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</tr>
<tr>
<td>Age, yr</td>
<td>9.6 ± 1.9</td>
<td>9.5 ± 1.9</td>
<td>9.7 ± 1.9</td>
<td>9.6 ± 1.8</td>
<td>0.9</td>
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<td>Male gender, N (%)</td>
<td>74 (73.3)</td>
<td>25 (71.4)</td>
<td>25 (64.1)</td>
<td>24 (88.9)</td>
<td>0.08</td>
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<tr>
<td>Body height, cm</td>
<td>135.2 ± 12.3</td>
<td>132.9 ± 11.3</td>
<td>135.7 ± 12.1</td>
<td>137.3 ± 13.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>35.7 ± 11.6</td>
<td>33.7 ± 10.6</td>
<td>34.8 ± 11.3</td>
<td>39.6 ± 12.7</td>
<td>0.1</td>
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<td>Body mass index, kg/m²</td>
<td>19.1 ± 3.7</td>
<td>18.7 ± 3.6</td>
<td>18.4 ± 3.7</td>
<td>20.4 ± 3.5</td>
<td>0.06</td>
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<tr>
<td>Body mass index z score ‡</td>
<td>0.8 ± 1.0</td>
<td>0.8 ± 1.1</td>
<td>0.60 ± 1.1</td>
<td>1.24 ± 0.8</td>
<td>0.04</td>
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<tr>
<td>Body surface area, m²</td>
<td>1.1 ± 0.2</td>
<td>1.1 ± 0.2</td>
<td>1.1 ± 0.2</td>
<td>1.2 ± 0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>104.7 ± 11.7</td>
<td>102.6 ± 11.9</td>
<td>104.2 ± 10.5</td>
<td>108.2 ± 12.8</td>
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<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>68.0 ± 9.7</td>
<td>67.3 ± 9.7</td>
<td>66.9 ± 10.5</td>
<td>70.6 ± 8.4</td>
<td>0.3</td>
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<tr>
<td><strong>Polysomnographics</strong></td>
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<tr>
<td>Sleep efficiency, %</td>
<td>81.1 ± 11.2</td>
<td>82.3 ± 8.7</td>
<td>80.3 ± 11.0</td>
<td>80.8 ± 14.2</td>
<td>0.7</td>
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<td>Apnoea-hypopnoea index, /hr † ‡</td>
<td>1.9 (0.5–5.5)</td>
<td>0 (0–0.6)</td>
<td>2.1 (1.4–3.0)</td>
<td>10.2 (6.9–17.3)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Oxygen desaturation index, /hr † ‡</td>
<td>0.4 (0–1.6)</td>
<td>0 (0–0.2)</td>
<td>0.5 (0.2–1.1)</td>
<td>4.0 (2.3–9.5)</td>
<td>&lt;0.0001</td>
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<td>Arousal index, /hr † ‡</td>
<td>6.8 (5.1–9.5)</td>
<td>5.8 (3.7–7.2)</td>
<td>6.0 (4.9–8.0)</td>
<td>10.3 (8.0–14.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Oxyhemoglobin saturation nadir, % † ‡</td>
<td>91.3 ± 3.9</td>
<td>93.6 ± 2.2</td>
<td>91.4 ± 1.9</td>
<td>88.1 ± 5.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Parametric data and non-parametric data were showed as mean ± SD and median (IQR) respectively.

* p < 0.05, Normal group vs Mild OSA group

† p < 0.05, Normal group vs Moderate-to-severe OSA group

‡ p < 0.05, Mild OSA group vs Moderate-to-severe OSA group.
Table 2. Group Comparisons of Right and Left Ventricular Structure and Function.

<table>
<thead>
<tr>
<th></th>
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<th>Reference (N = 35)</th>
<th>Mild OSA (N = 39)</th>
<th>Moderate-to-severe OSA (N = 27)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Right Ventricle (RV)</strong></td>
<td></td>
<td></td>
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<tr>
<td>RV systolic volume index, ml/m *†</td>
<td>0.23 ± 0.09</td>
<td>0.18 ± 0.08</td>
<td>0.26 ± 0.10</td>
<td>0.25 ± 0.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV ejection fraction, % *†</td>
<td>53.4 ± 12.5</td>
<td>59.3 ± 11.0</td>
<td>51.4 ± 12.3</td>
<td>48.7 ± 11.9</td>
<td>0.001</td>
</tr>
<tr>
<td>RV myocardial performance index † ‡</td>
<td>0.37 ± 0.12</td>
<td>0.32 ± 0.09</td>
<td>0.36 ± 0.09</td>
<td>0.46 ± 0.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Left Ventricle (LV)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV systolic volume index, ml/m</td>
<td>22.6 ± 9.6</td>
<td>23.0 ± 9.8</td>
<td>23.0 ± 8.9</td>
<td>21.4 ± 10.5</td>
<td>NS</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>66.2 ± 10.7</td>
<td>66.3 ± 10.1</td>
<td>64.4 ± 10.0</td>
<td>68.6 ± 12.1</td>
<td>NS</td>
</tr>
<tr>
<td>LV mass index, g/m².⁷</td>
<td>32.6 ± 9.5</td>
<td>32.5 ± 7.8</td>
<td>30.3 ± 7.3</td>
<td>36.3 ± 12.9</td>
<td>0.04</td>
</tr>
<tr>
<td>Relative wall thickness ‡</td>
<td>0.36 ± 0.07</td>
<td>0.36 ± 0.07</td>
<td>0.34 ± 0.06</td>
<td>0.39 ± 0.07</td>
<td>0.005</td>
</tr>
<tr>
<td>Interventricular septal thickness index, cm/m ‡</td>
<td>0.56 ± 0.09</td>
<td>0.56 ± 0.09</td>
<td>0.52 ± 0.09</td>
<td>0.60 ± 0.09</td>
<td>0.004</td>
</tr>
<tr>
<td>LV posterior wall thickness index, cm/m</td>
<td>0.52 ± 0.10</td>
<td>0.52 ± 0.10</td>
<td>0.50 ± 0.09</td>
<td>0.56 ± 0.11</td>
<td>NS</td>
</tr>
<tr>
<td>Abnormal LV Geometry, N (%) §</td>
<td>43 (42.6)</td>
<td>14 (40.0)</td>
<td>9 (23.1)</td>
<td>20 (74.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV myocardial performance index</td>
<td>0.33 ± 0.11</td>
<td>0.32 ± 0.08</td>
<td>0.32 ± 0.12</td>
<td>0.35 ± 0.14</td>
<td>NS</td>
</tr>
<tr>
<td>E/A (mitral valve)</td>
<td>2.2 ± 1.6</td>
<td>2.0 ± 0.6</td>
<td>2.6 ± 2.5</td>
<td>2.0 ± 0.4</td>
<td>NS</td>
</tr>
<tr>
<td>E/e’ † ‡</td>
<td>9.5 ± 1.8</td>
<td>9.1 ± 1.8</td>
<td>9.3 ± 1.4</td>
<td>10.4 ± 2.1</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Data are showed as mean ± SD unless otherwise specified.

Definition of abbreviations: E/A = ratio of early to late peak transtricuspid or transmitral flow; E/e’, ratio of mitral early peak velocity / mitral annulus early peak velocity.

* p < 0.05, Normal group vs Mild OSA group
† p < 0.05, Normal group vs Moderate-to-severe OSA group
‡ p < 0.05, Mild OSA group vs Moderate-to-severe OSA group
§ p < 0.016, for Normal group vs Moderate-to-severe OSA group and Mild OSA group vs Moderate-to-severe OSA group.
Table 3. Multiple linear regression analyses showing the association between PSG and ECHO parameters after adjustment for age, gender and body mass index z score.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Log-transformed AHI</th>
<th></th>
<th>Log-transformed ODI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β [95% CI]</td>
<td>Sig.</td>
<td>β [95% CI]</td>
<td>Sig.</td>
</tr>
<tr>
<td>Right ventricle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic volume index</td>
<td>1.6 [0.8 – 2.5]</td>
<td>0.0002</td>
<td>1.2 [0.2 – 2.1]</td>
<td>0.017</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>-2.7 [(-4.0) – (-1.3)]</td>
<td>0.0001</td>
<td>-2.0 [(-3.5) – (-0.5)]</td>
<td>0.009</td>
</tr>
<tr>
<td>Myocardial performance index</td>
<td>0.033 [0.021 – 0.046]</td>
<td>&lt;0.0001</td>
<td>0.025 [0.011 – 0.040]</td>
<td>0.0007</td>
</tr>
<tr>
<td>Left ventricle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular mass index</td>
<td>0.31 [-0.78 – 1.39]</td>
<td>NS</td>
<td>0.62 [-0.54 – 1.78]</td>
<td>NS</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.003 [-0.006 – 0.011]</td>
<td>NS</td>
<td>0.006 [-0.003 – 0.015]</td>
<td>NS</td>
</tr>
<tr>
<td>Interventricular septal thickness index</td>
<td>0.007 [-0.004 – 0.018]</td>
<td>NS</td>
<td>0.015 [0.003 – 0.026]</td>
<td>0.016</td>
</tr>
<tr>
<td>E/e’</td>
<td>0.21 [0 – 0.42]</td>
<td>0.05</td>
<td>0.17 [-0.05 – 0.40]</td>
<td>NS</td>
</tr>
</tbody>
</table>

Definition of abbreviations: β (95% CI) = beta coefficient (95% confidence intervals); AHI = apnoea-hypopnoea index; ODI = oxygen desaturation index; NS = not significant; E/e’ = ratio of mitral early peak velocity / mitral annulus early peak velocity
**Table 4. Intra- and inter-group comparisons between the effectively treated group and the ineffectively treated group**

<table>
<thead>
<tr>
<th></th>
<th>Persistent OSA  (Δ AHI &gt; –50%)</th>
<th>Improved OSA  (Δ AHI &lt; –50%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N = 19</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age at baseline, yr</strong></td>
<td>8.8 (7.5, 9.4)</td>
<td>9.8 (8.2, 11.1)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Body mass index z score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.41 (0.67, 1.78)</td>
<td>0.84 (-0.15, 1.82)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>1.63 (0.76, 1.78)</td>
<td>0.63 (-0.20, 1.82)</td>
<td>NS</td>
</tr>
<tr>
<td>*P value</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>0.04 (-0.20, 0.22)</td>
<td>0.10 (-0.13, 0.22)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Apnoea-hypopnoea index, hr⁻¹</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>3.0 (2.3, 6.9)</td>
<td>10.2 (2.6, 17.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>6.0 (2.8, 7.8)</td>
<td>0.8 (0.3, 3.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>*P value</td>
<td>NS</td>
<td>0.0003</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>1.5 (-0.5, 4.2)</td>
<td>-7.0 (-15.3, -2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>RV ejection fraction, %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>51.5 (43.4, 60.3)</td>
<td>47.2 (42.7, 58.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>50.5 (36.7, 58.3)</td>
<td>55.5 (45.1, 60.4)</td>
<td>NS</td>
</tr>
<tr>
<td>*P value</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-1.9 (-9.3, 3.5)</td>
<td>1.7 (-1.9, 12.5)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>RV myocardial performance index</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.354 (0.321, 0.414)</td>
<td>0.490 (0.408, 0.555)</td>
<td>0.011</td>
</tr>
<tr>
<td>Follow-up</td>
<td>0.337 (0.288, 0.430)</td>
<td>0.354 (0.288, 0.402)</td>
<td>NS</td>
</tr>
<tr>
<td>*P value</td>
<td>NS</td>
<td>0.025</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-0.03 (-0.16, 0.10)</td>
<td>-0.11 (-0.25, 0.04)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Relative wall thickness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.338 (0.302, 0.376)</td>
<td>0.372 (0.319, 0.464)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>0.377 (0.333, 0.418)</td>
<td>0.372 (0.311, 0.404)</td>
<td>NS</td>
</tr>
<tr>
<td>*P value</td>
<td>NS</td>
<td>0.039</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>0.014 (-0.002, 0.074)</td>
<td>-0.017 (-0.063, 0.001)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Interventricular septal thickness index, cm/m</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.507 (0.490, 0.633)</td>
<td>0.606 (0.500, 0.661)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>0.540 (0.440, 0.648)</td>
<td>0.528 (0.500, 0.577)</td>
<td>NS</td>
</tr>
<tr>
<td>*P value</td>
<td>NS</td>
<td>0.022</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-0.008 (-0.070, 0.120)</td>
<td>-0.036 (-0.097, -0.008)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>E/e’</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>9.3 (8.7, 9.9)</td>
<td>10.2 (8.8, 12.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>9.4 (8.9, 11.2)</td>
<td>9.1 (8.4, 9.9)</td>
<td>NS</td>
</tr>
<tr>
<td>*P value</td>
<td>NS</td>
<td>0.013</td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>0.3 (-0.8, 1.7)</td>
<td>-1.4 (-3.2, -0.1)</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>Abnormal LV geometry, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>7 (36.8)</td>
<td>10 (58.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>10 (52.6)</td>
<td>8 (47.1)</td>
<td>NS</td>
</tr>
<tr>
<td>*P value</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Acquired abnormal LV geometry, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>6 (31.6)</td>
<td>2 (11.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up</td>
<td>3 (15.8)</td>
<td>4 (23.5)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are showed as median (IQR) unless otherwise specified.

Definition of abbreviations: AHI = apnoea-hypopnoea index; RV = right ventricle; E/e’ = ratio of mitral early peak velocity / mitral annulus early peak velocity

* P values were obtained from Wilcoxon Signed Ranks tests (intra-group comparisons).
Cardiac Remodeling and Dysfunction in Children with Obstructive Sleep Apnea - A Community Based Study

Yat-sun YS Chan, Albert M Li, Chun-ting Au, Amy FC Lo, Siu-kwan Ng, Victor J Abdullah, Crover Ho, Cheuk-man Yu, Tai-fai Fok and Yun-kwok Wing

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