BP and Arterial Distensibility in Children With Primary Snoring*

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Study objective: **While previous studies have suggested an association between obstructive sleep apnea and cardiovascular complications, the effects of primary snoring in children on daytime systemic BP and arterial distensibility remain unknown.**
Design and patients: **To determine the effects of primary snoring on BP and peripheral conduit artery distensibility, 30 children with primary snoring were studied at an age of 9.5 ± 2.8 years (mean ± SD). Systemic BP was measured using an automated device, while brachioradial arterial distensibility was assessed by measuring pulse wave velocity (PWV), which is inversely related to the square root of distensibility. The results were compared to those of 30 healthy control subjects matched for age, sex, and body size.**
Results: **As compared to control subjects, children with primary snoring had significantly higher systolic BP (112 ± 10 mm Hg vs 105 ± 8 mm Hg, p = 0.001), diastolic BP (60 ± 7 mm Hg vs 53 ± 9 mm Hg, p = 0.004), and mean BP (81 ± 7 mm Hg vs 71 ± 8 mm Hg, p < 0.001). Likewise, those with primary snoring had significantly higher PWV (9.7 ± 1.6 m/s vs 7.9 ± 2.0 m/s, p = 0.001). Multiple regression identified age, body mass index (BMI), and primary snoring as significant determinants of systemic BP; however, primary snoring is the only significant determinant of PWV. Regardless of the BMI, systemic BP and PWV remained significantly higher in children with primary snoring.**
Conclusion: **Children with primary snoring have increased daytime systemic BP and reduced arterial distensibility, which may jeopardize long-term cardiovascular health.**
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Key words: arterial distensibility; BP; snoring

Abbreviations: BMI = body mass index; PWV = pulse wave velocity

Snoring affects up to 10% of children.[1–3] It is a nondiscriminating presenting symptom of sleep-related disorders, a continuum that starts from primary snoring without obstructed breathing to the opposite extreme of obstructive sleep apnea.[4] Previous studies in children and adults suggest associations between obstructive sleep apnea and cardiovascular complications,[5–11] the strongest being its association with systemic hypertension. Although a causal relationship has not been established, one animal study[12] suggested an etiologic link between the two. In contrast, the association between primary snoring and cardiovascular morbidity in adults has been controversial.[13] This in part is related to strong confounding influence of other cardiovascular risk factors in adulthood,[13] complete elimination of which might be difficult if not impossible.[14] The pediatric population would therefore, in this regard, be a better cohort for clearer definition of possible associations. Nevertheless, to date, no studies have yet been performed in children to examine specifically the effect of primary snoring on systemic BP. The potential clinical implication of a link, if indeed demonstrable, is significant as primary snoring in children is currently regarded as relatively benign and that interventions can safely be deferred.[15]

Proposed mechanisms underlying development of hypertension in adults with sleep-related disorders include an increase in vasoconstrictors and an enhanced sympathetic tone.[16–18] The end result of such disturbances in vasomotor control may be translated functionally into alteration of the distensibility of the

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arteries. The significance of arterial distensibility is in its direct relation to characteristic impedance of blood vessels, which has been regarded as an index of pulsatile cardiac afterload.[19] Arterial distensibility can satisfactorily be estimated *in vivo* by measuring the pulse wave velocity (PWV),[20] which is inversely related to the square root of arterial distensibility. Hence, the less distensible the arterial segment, the faster the PWV.

Given the prevalence of snoring in children and the potential association of sleep-related disorders with cardiovascular complications, it is important to clarify their interrelationships. In this study, the daytime systemic BP and peripheral conduit arterial distensibility, as assessed by PWV, in children with primary snoring were determined and compared to those in normal children matched for age, sex, and body size.

Materials and Methods

Study Subjects

Thirty children with diagnosed primary snoring were recruited. Children who snore but do not demonstrate apnea or hypoventilation on polysomnography are considered to have primary snoring.[15] All underwent polysomnography, as described below, to exclude obstructive sleep apnea. Thirty healthy children matched for age, sex, and body size were recruited as control subjects. The absence of snoring in the control subjects was confirmed by parental interviews. The institutional Ethics Committee approved the study, and parents of all subjects gave written, informed consent.

In all subjects, the body weight and height were measured, and the body mass index (BMI) was calculated. The daytime systemic BP was measured twice in the right upper arm using an automatic oscillometric device (Dinamap; Critikon; Tampa, FL) after at least 10 min of rest, with the subjects in the seated position, and the mean reading was used for subsequent analyses.

Polysomnography

Polysomnographic studies were performed overnight in a single room in all 30 patients. No sedation or sleep deprivation was used. Continuous video recording using an infrared video camera was performed after obtaining written consent from the parents. The polysomnogram consisted of multichannel recordings of the following parameters: four EEG tracings, right and left electrooculographic tracings, submental electromyogram, tibial electromyogram, ECG, snoring sound (microphone), oronasal airflow (three-pronged thermistor), chest and abdominal wall motion (piezoelectric transducers), and systemic oxygen saturation (Healthdyne Oximeter model 930; Respironics; Murrysville, PA). All data were stored for off-line analysis. Primary snoring was diagnosed in children who snored but did not show significant apnea or hypopnea on the polysomnogram.[15] An apnea-hypopnea index, the number of obstructive apneas and hypopneas per hour of sleep,[11] of ≤ 1 was used for defining this patient group.

PWV

Each subject rested in supine position for at least 10 min before recordings were made. The PWV in the brachioradial arterial segment was measured by a previously validated noninvasive photoplethysmographic technique.[20–21] Briefly, two probes, each containing an infrared-emitting diode and a phototransistor, were placed over the right brachial and right radial arteries and secured without compression. As the pulse wave passes along and distends the artery under the probe, more of the infrared signal is absorbed and less reflected. The signals from the two probes were amplified, displayed in real time on the monitor, and sampled by an analog-to-digital converter. Three recordings were stored digitally for subsequent off-line analysis. The transit time was determined from the time delay between the foot of the corresponding brachial and radial pulse waves. The PWV was derived by dividing the measured distance between the two probes by the transit time.

Data Analysis

Data are presented as mean ± SD unless otherwise stated. Differences in anthropometric data, systemic BP, and PWV between patients and control subjects were compared using paired Student *t* test. Linear regression was performed to assess relation between systemic BP and BMI in the two groups, and the two regression lines were compared using analysis of covariance. Stepwise multiple linear regression was used to identify significant determinants of PWV and systemic BP for the entire cohort. A p value of < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 10.0 (SPSS; Chicago, IL).

Results

Subjects

Thirty children (18 boys) who had primary snoring were studied at an age of 9.5 ± 2.8 years. They had a body weight of 37.8 ± 13.3 kg (range, 19.7 to 66.0 kg) and a BMI of 19.5 ± 3.6 (range, 14.2 to 26.8). The school performance, as rated by their parents, was good in 4 patients, fair in 18 patients, and poor in 8 patients. None of the patients were receiving vasoactive medications at the time of study. Family history of cardiovascular disease was present in three patients, whose paternal grandparent had coronary artery disease. Thirty healthy control subjects matched for age, sex, body weight, and height were recruited from the local schools. The anthropometric data of all the subjects are summarized in Table 1.

Systemic BP

Children with primary snoring had significantly higher daytime systolic BP (112 ± 10 mm Hg vs 105 ± 8 mm Hg, $p = 0.001$) and diastolic BP (60 ± 7 mm Hg vs 53 ± 9 mm Hg, $p = 0.004$), as compared to the matched control subjects (Fig 1). Likewise, the mean BP in the patients was significantly higher (81 ± 7 mm Hg vs 71 ± 8 mm Hg, $p < 0.001$).

Table 1—*Anthropometric Data of Patients and Control Subjects

Variables	Patients (n = 30)	Control Subjects (n = 30)	p Value
Age, yr	9.5 ± 2.8	9.7 ± 2.7	0.11
Weight, kg	37.9 ± 13.3	37.1 ± 12.4	0.47
Height, cm	137.0 ± 13.9	137.0 ± 14.0	0.98
BMI	19.53 ± 3.60	19.21 ± 3.52	0.07

*Data are presented as mean ± SD.

To identify determinants of systemic BP in the entire cohort of 60 subjects, the following dependent variables were included in the multivariate analysis by stepwise multiple linear regression: age, sex, gender, BMI, primary snoring status (present vs absent), and PWV (Table 2). For systolic and mean BPs, significant determinants were age, BMI, and primary snoring. For diastolic BP, only age and primary snoring were found to be significant.

To further determine the potential confounding influence of BMI on systemic BP in children with and without primary snoring, linear regression analyses of mean BP vs BMI for the two groups were performed (Fig 2). The slopes of the two regression lines were similar (0.9 ± 0.3 mm Hg/kg/m^2 vs 1.0 ± 0.4 mm Hg/kg/m^2, p = 0.81), but y-intercept of the regression line of patient group was significantly greater than that of control group (64 ± 7 mm Hg vs 51 ± 7 mm Hg, p < 0.001), suggesting that while mean BP increased with BMI in both groups, patients had significantly higher BP than control subjects throughout the range of BMI in this cohort.

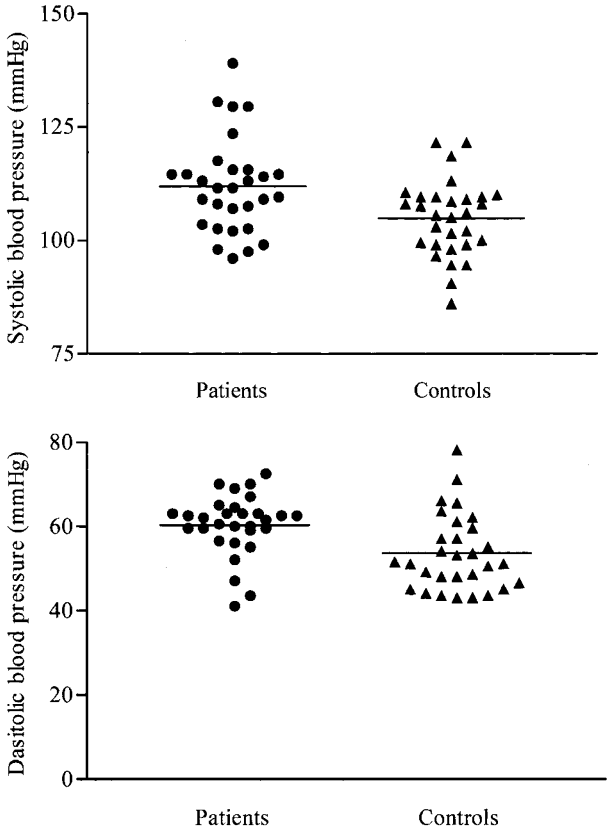

FIGURE 1. Systolic (*top*) and diastolic (*bottom*) BP in patients with primary snoring and control subjects. The horizontal lines represent the means in each group.

Table 2—*Determinants of Daytime Systemic BP*

Variables	Systolic BP β	Systolic BP p Value	Diastolic BP β	Diastolic BP p Value	Mean BP β	Mean BP p Value
Age, yr	1.28	0.002*	1.01	0.006*	0.909	0.007*
BMI	1.00	0.002*		0.25	0.613	0.019*
Primary snoring status (present)	6.98	0.001*	5.79	0.005*	9.039	< 0.001*
Male sex		0.21		0.07		0.07
Pulse wave velocity, m/s		0.99		0.16		0.32
Model R^2		0.48		0.32		0.56

*Statistically significant.

PWV

The brachioradial PWV was significantly higher in children with primary snoring (9.7 ± 1.6 m/s vs 7.9 ± 2.0 m/s, p = 0.001), as compared to control subjects (Fig 3). Dependent variables entered into the multivariate model for identification of significant determinants of PWV were age, sex, gender, BMI, systemic BP, and primary snoring status. Primary snoring was the only identifiable significant determinant of PWV in this cohort (β = 1.96, p < 0.001; model R^2 = 0.26).

To further define the potential confounding influence of BMI on PWV, as described previously,[22] the cohort was further subcategorized using a BMI of 19 as a cutoff point, which approximated to the median BMI of the whole cohort. The influence of BMI on PWV in patients and control subjects is shown in Figure 4. The PWV remained significantly higher in children with primary snoring regardless of whether the BMI was ≤ 19 (p = 0.005) or > 19 (p = 0.03). Furthermore, the difference of 2.3 ± 2.7 m/s in PWV between patients and control subjects with BMI ≤ 19 was similar to that between patients and control subjects with BMI > 19 (1.6 ± 2.6 m/s, p = 0.51).

DISCUSSION

To the best of our knowledge, this is the first study to assess the effects of primary snoring on systemic

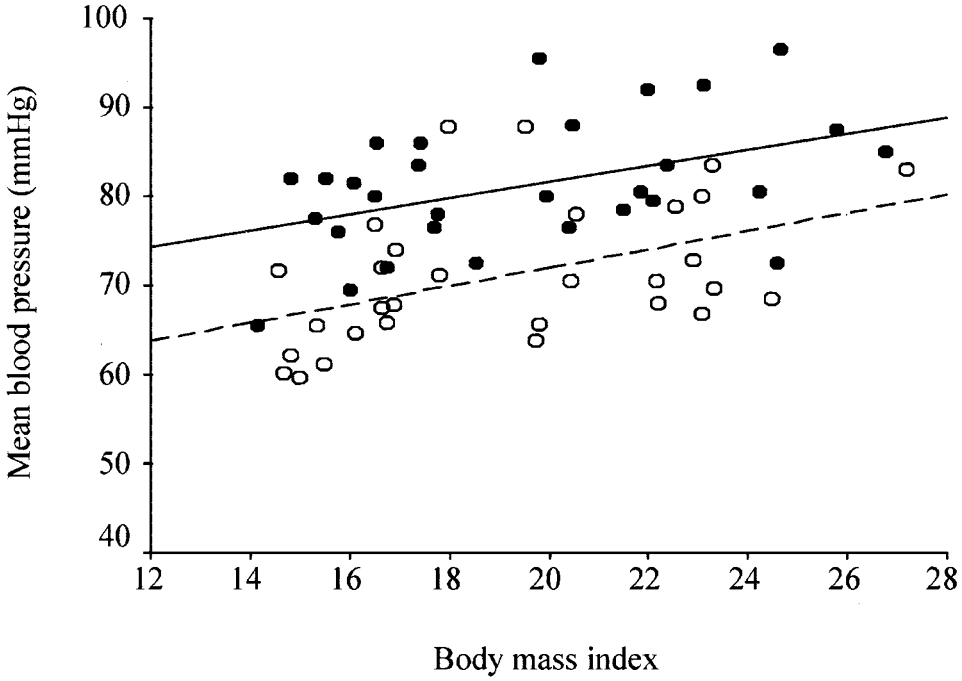

FIGURE 2. Linear regression of mean systemic BP on BMI in patients (closed circles) and control subjects (open circles).

BP and arterial distensibility in children. Our study demonstrates that children with primary snoring have significantly higher daytime systemic BP and lower arterial distensibility. Significant determinants of systemic BP identified in this cohort are age, BMI, and primary snoring; however, primary snoring is the only identifiable significant determinant of arterial distensibility. The potential confounding influence of BMI on both of these indexes is minimized by recruiting control subjects who are matched for body size, using a multivariable model in statistical analysis of data, and further subdividing the cohort based on BMI for analysis.

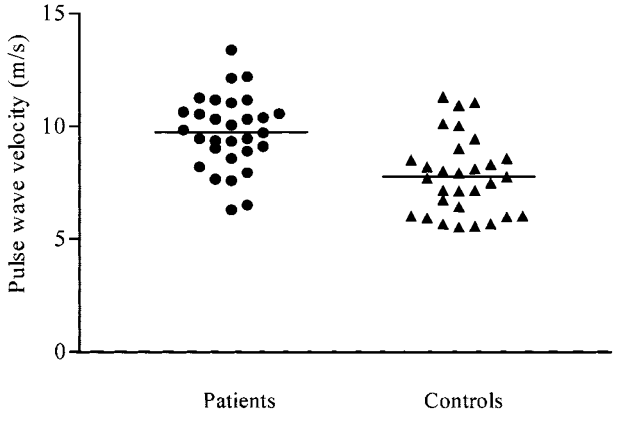

FIGURE 3. PWV in patients with primary snoring and control subjects. The horizontal lines represent the means in each group.

While associations between obstructive sleep apnea, the opposite extreme of the spectrum of sleep-disordered breathing, and cardiovascular morbidities have been reported extensively,[5–9] the relationship between snoring and cardiovascular complications remains controversial.[13–19] Hoffstein[13] summarized in a very thorough review the results of 19 adult studies with controversial conclusions, and opined that evidence to date does not support the conclusion that snoring is an independent risk factor for adverse vascular complications. Nonetheless, important limitations of the quoted studies were also highlighted, including the failure to adjust confounding factors by multivariate analysis, the lack of polysomnography to eliminate confounding effects of sleep apnea, and the different definitions of snoring. In a more controlled study by Young et al,[23] in which all subjects underwent overnight polysomnography, adults with simple snoring had increased morning and evening BP even after adjusting for age, sex, and BMI. Given the strong association between sleep-related disorders and confounding factors in adults, even in studies controlling for confounding factors, there persists a potential for residual confounding. The pediatric population might therefore be a better cohort for clearer definition of the issue in this regard.

Limited data are available in the pediatric literature. Marcus et al[11] showed that children with obstructive sleep apnea had significantly higher dia-

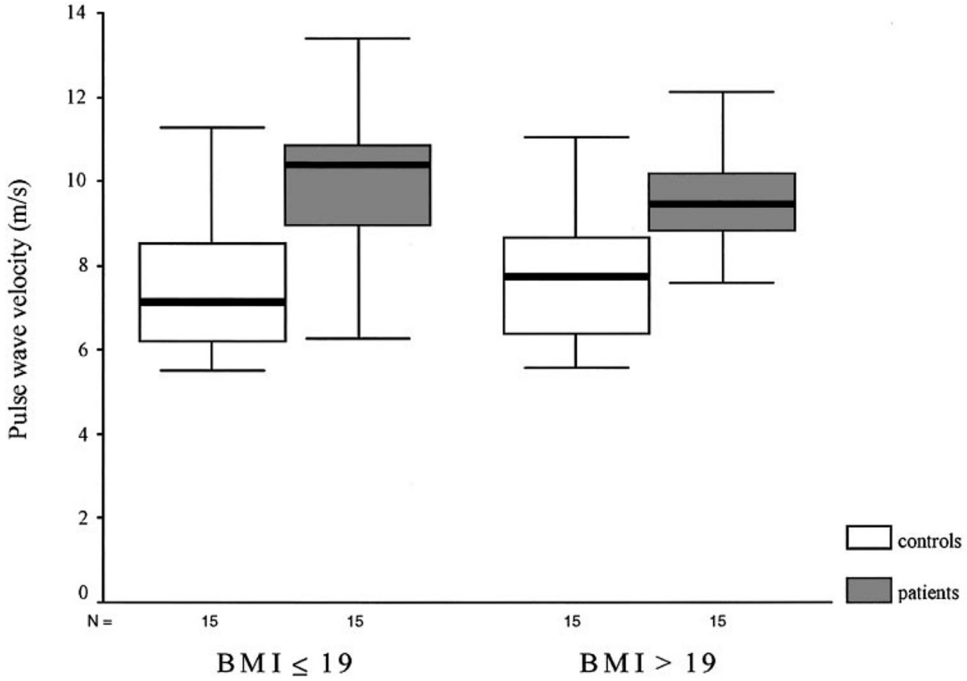

FIGURE 4. Clustered box plots of PWV by BMI of patients and control subjects. The lines within the box represent the medians in each group.

stolic BP than those with primary snoring. When compared with normative data, 32% (13 of 41 subjects) with sleep apnea and 19% (5 of 21 patients) with primary snoring had either systolic or diastolic pressure > 95th centile during either sleep or wakefulness. Nonetheless, the BP readings in their subjects, obtained from an automated oscillometric device, were compared to normative data that were obtained by auscultatory method.[24] Park et al[25] showed in a large cohort of children that oscillometric systolic and diastolic readings were 10 mm Hg and 5 mm Hg higher that the auscultatory systolic pressure and Korotkoff phase V diastolic pressure reading, respectively. Thus, interchange and comparison of readings obtained by the two different methods are hence unlikely to be valid. In this study, we therefore compared the BP readings in patients to those obtained in control subjects using the same oscillometric method.

Our findings demonstrate that children with primary snoring had significantly higher daytime systolic, diastolic, and mean BP than those of healthy control subjects. While obesity may confound the association, primary snoring remains significant after adjustment for BMI. The mechanism underlying the observed increase in systemic BP in this cohort remains speculative. A previous adult study[23] demonstrated stepwise increase in systolic and diastolic BP, adjusted for possible confounding variables, across categories of no sleep-related breathing, simple snoring, and increasing severity along the sleep-related breathing spectrum. Hence, it appears possible that mechanisms operating in the development of sustained hypertension in patients with obstructive sleep apnea might also be operating in those with primary snoring, but with a dose-dependent effect. Proposed mechanisms underlying development of hypertension in adults with sleep-related disorders included an increase in vasoconstrictors including catecholamine and endothelin and an enhanced sympathetic tone.[16–18,26] Such abnormalities have been demonstrated not only during sleep and apneic events, but also during waking periods.[16–18] The observation that arterial distensibility is significantly reduced in our patients may be a reflection of such an increase in arterial tone.

Arterial distensibility is an important mechanical property as it is related to the impedance of blood vessels and in turn to the pulsatile afterload that is presented to the left ventricle.[19] Studies[27] suggest that decreased arterial distensibility, as assessed by PWV, is a strong independent predictor of cardiovascular morbidity and mortality in patients with hypertension. Although PWV may vary with systemic BP,[28] we[29] and others[30] have shown that changes in PWV in vasculitis and with aging, respectively, are not entirely attributable to changes in systemic BP. The fact that systemic BP is not a significant determinant of PWV in the present cohort further suggests that the increase in PWV is indicative of a genuine decrease in arterial distensibility rather than

acting as a surrogate marker of an increase in systemic BP. Chronic increase in cardiac afterload may hence jeopardize the long-term cardiovascular health of this group of patients.

It is possible that some of our subjects had upper airway resistance syndrome rather than simple primary snoring, as esophageal pressure and end-tidal carbon dioxide were not monitored during the sleep studies. Nevertheless, efforts have been made to scrutinize for obvious thoracoabdominal asynchrony from the polysomnogram and respiratory distress from video recordings, with exclusion of patients manifesting these abnormalities. A mild degree of snoring in the control subjects might have escaped detection by their parents. However, the effect of missing control subjects with snoring is lowering the possibility of finding a difference in systemic BP and arterial distensibility between patients and healthy children, rather than falsely demonstrating a significant difference.

Primary snoring has been regarded as relatively benign, because it does not progress to frank obstructive sleep apnea in the majority of children.[15,31] Based on this clinical course, it has also been suggested that deferment of treatment is safe.[15] Nevertheless, this approach may perhaps warrant critical reappraisal in the light of our findings, as long-term cardiovascular health may be jeopardized by chronic elevation of systemic BP and reduction of arterial distensibility. We therefore recommend regular outpatient monitoring of BP and arterial distensibility in these at-risk children, and early institution of therapy for those with evidence of disturbance in vascular function.

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