The prevalence of obstructive sleep apnoea and its association with aortic dilatation in Marfan’s syndrome

Malcolm Kohler, MD¹, Edward Blair, MD, MRCP², Peter Risby²,
Annabel H Nickol, PhD, MRCP¹, Paul Wordsworth, MB, FRCP³, Colin Forfar, MD,
FRCP⁴, John R Stradling, MD, FRCP¹

¹ Oxford Centre for Respiratory Medicine, Churchill Hospital, Oxford, UK
² Department of Clinical Genetics, Churchill Hospital, Oxford, UK
³ Department of Clinical Rheumatology, Nuffield Orthopaedic Hospital, Oxford, UK
⁴ Department of Cardiovascular Medicine, John Radcliffe Hospital, Oxford, UK

Total word count: 2819
Abstract word count: 231
Key words: Marfan’s syndrome, sleep apnoea, aortic dilatation, prevalence

Licence for publication: the corresponding author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence on a worldwide basis to the BMJ Publishing Group Ltd and its licencees, to permit this article (if accepted) to be published in Thorax and any other BMJ Group products and to exploit all subsidiary right as set out in the licence (http://thorax.bmjjournals.com/ifora/licence.pdf.

Correspondence:
Malcolm Kohler, MD
Oxford Centre for Respiratory Medicine
Oxford Radcliffe Hospitals, Churchill Hospital Campus
Headington, Oxford, OX3 7LJ, United Kingdom
Phone: 0044-1-865 225 227
Fax: 0044-1-865 225 221
E-mail: Malcolm.K@bluewin.ch
Abstract

**Background** : Craniofacial abnormalities and increased pharyngeal collapsibility due to abnormal connective tissue suggest the possibility of an increased prevalence of obstructive sleep apnoea (OSA) in patients with Marfan’s syndrome, but the actual prevalence is uncertain. Aortic dilatation and dissection are life-threatening manifestations of Marfan’s syndrome and case reports have suggested a possible association with OSA, but data from cohort studies are not available.

**Methods** : A sleep study was performed in 61 patients with Ghent-criteria positive Marfan’s syndrome (mean age±SD, 38.3±12.9, 37 females) and in 26 control subjects matched for age, gender, height and weight. OSA was defined using two conventional levels of apnoea/hypopnoea index (AHI), >5 and >15 per hour. In patients with Marfan’s syndrome aortic root diameter was measured by echocardiography.

**Results** : More patients with Marfan’s syndrome than controls had OSA (AHI >5, 32.8% compared to 11.5%, mean difference +21.3%, 95% CI 4.2-38.3%, p=0.04, AHI >15, 18.0% compared to 0%, mean difference +18.0%, 95% CI 8.4-27.7%, p=0.02). AHI was correlated with aortic root diameter (r=0.50, 95% CI 0.26-0.69, p=0.0003), and mean±SD aortic root diameter was significantly greater in patients with OSA (4.5±0.6cm) compared to those without OSA (3.7±0.6cm) (mean difference 0.8cm, 95% CI 0.4-1.2 cm, p<0.0001).

**Conclusions** : In patients with Marfan’s syndrome the prevalence of OSA is considerably higher than in matched control subjects. OSA may be a risk factor for aortic root dilatation in Marfan’s syndrome.
Introduction

Marfan’s syndrome is an autosomal dominant inherited multisystem disorder. It is caused by mutations in the FBN1 gene localized on chromosome 15q21, which encodes the matrix protein fibrillin 1. The incidence of Marfan’s syndrome is estimated to be 2-3 per 10000 individuals. [1] To date there is no rapid and efficient molecular diagnostic test to identify individuals with the disease, thus the diagnosis primarily depends on a combination of major and minor clinical findings defined in the “Ghent criteria”. [2,3] The hallmark clinical features are noted in the cardiovascular, ocular, and skeletal systems.

Aortic root dilatation and subsequent dissection are the commonest life-threatening manifestations of Marfan’s syndrome. Dilatation of the aortic root can begin in childhood or early adulthood and increases at an unpredictable rate. [4,5] It is still a matter of debate which factors contribute to a rapid progression of aortic root dilatation.

The high prevalence of craniofacial dysmorphisms and an increased upper airway collapsibility [6] could predispose to an increased prevalence of obstructive sleep apnea (OSA) in patients with Marfan’s syndrome, however there is only very limited information in the literature concerning the actual prevalence of OSA in this patient group. Cistulli and Sullivan [7] reported a prevalence of 64% (defined by a AHI>5), but the interpretation of this finding is limited as only 25 subjects with Marfan’s syndrome were included in the study.

A possible causal link between OSA and aortic dilatation in patients with Marfan’s syndrome has been suggested in two case reports. [8,9] Possible underlying pathophysiological mechanisms are post-apnea reflex sympathetic activation and consequent marked increases in blood pressure [10], which produce shear stresses in
blood vessel walls – forces that are thought to cause vascular wall damage. [11] Furthermore, largely negative intrathoracic pressure swings, which are produced during obstructive apneas, increase transaortic pressures [12], and may therefore accelerate aortic dilatation. To date, there are no data from cohort studies that have investigated the possible association of OSA with aortic root dilatation in patients with Marfan’s syndrome.

We have addressed this issue by performing a case-control study to evaluate the prevalence of OSA, and its possible correlation with aortic root dilatation in a large cohort of patients with Marfan’s syndrome.

**Methods**

**Patients and controls**

Patients fulfilling the Ghent criteria [2,3] for Marfan’s syndrome and attending their yearly clinical assessment at our institution were asked to participate in the study. Control subjects were recruited from the local population by an advertisement which was placed in the Oxford Radcliffe Hospitals NHS Trust sites and selected from amongst the volunteers to match subjects with Marfan’s syndrome as closely as possible for average/frequency of age, gender, height and weight in order to compare the prevalence of OSA. Subjects were eligible if they were between 18 and 75 years old, not pregnant, and not treated with continuous positive airway pressure (CPAP). The study was approved by the Oxford research ethics committee (REC No 07/Q1607/6), and written informed consent was obtained from all participants.
Measurements

*Anthropometrics and blood pressure*

The following anthropometrical parameters were measured in all participants: height, weight, neck circumference, crico-mental distance, palatal height, maxillary and mandibular intermolar distance by callipers according to the method described by Kushida et al. [13] Tonsillar enlargement was assessed as previously described (Class I: tonsils absent, class II: tonsils do not extend beyond the palatopharyngeal arch, class III: tonsils at the palatopharyngeal arch, class IV: tonsils extend beyond the palatopharyngeal arch). [14] Palatal position or tongue size was assessed by the Mallampati-score (Class I: all the oropharynx including tonsils, pillars, soft palate and tip of uvula are visible, class II: tonsils’ upper pole and uvula visible, class III: part of the uvula and soft palate visible, class IV: hard palate and part of soft palate are barely visible). [15,16] The facial profile was categorized as retrognathic, neutral, or prognathic in Frankfurt position) [17] and the dental overbite was measured by a calliper as previously described. [14]

Blood pressure and heart rate were measured in the sitting position with a standard digital automatic monitor (Omron Healthcare Company, Kyoto, Japan). The mean value of three readings was used for analysis.

*Sleep studies and questionnaire*

Subjective sleepiness was assessed using the Epworth Sleepiness Scale (ESS) questionnaire. Home sleep studies were performed using the ApneaLink™ device (ResMed, MAP medicine technology, Martinsried, Germany). The device records the patient’s nasal respiratory pressure signal and finger oximetry during sleep; and has been validated as an accurate instrument to detect snoring, apnoea/hypopnoea and oxygen desaturations. [18] The results of the sleep study were scored automatically.
with dedicated software (ResMed, MAP medicine technology, Martinsried, Germany), with manual review to ensure accuracy of the data. Apnoeas were defined as a cessation of airflow lasting > 10 seconds, and hypopnoeas as a reduction in airflow of at least 50% lasting > 10 seconds, associated with a drop in oxygen saturation of >4%. Snoring severity was quantified as the number of snoring events per hour of study. OSA severity was quantified as the number of apnoeas/hypopnoeas (AHI) and oxygen desaturations >4% per hour of study (ODI).

Aortic root diameter measurements

In all patients with Marfan’s syndrome echocardiography was performed by the same cardiac ultrasound technician, who was not involved in the analysis of the study. Aortic root diameter was measured in parasternal long-axis view at end-diastole (peak of R wave on electrocardiogram) and at end-systole (T wave on electrocardiogram) by two-dimensional, M-mode echocardiography with a commercially available cardiac ultrasound system (Sonos 4500, Philips Healthcare, UK), using a 3.5 MHz transducer. The diameter of the aorta was assessed at several levels: at the left ventricular outflow tract, sinuses of Valsalva, supra-aortic ridge, and at the proximal ascending aorta, 1 to 2 cm above the supra-aortic ridge as described previously. [19] The maximal diameter of the aortic root from these four assessments and the maximal diameter corrected for age and body surface area (predicted maximal diameter in %), were used for further statistical analysis. [19]

Data analysis

Data are expressed as means (SD). All statistical analyses were performed with Statistica V6.0 (StatSoft, Tulsa, OK, USA). Non normally distributed data were normalised by square root transformation for statistical analysis. Demographics, results of the sleep study and echocardiography were compared by independent $t$ tests.
In order to define the prevalence of OSA two conventional threshold levels of AHI, >5 and >15 per hour, were used. The threshold of >5 was also used for subgroup comparisons of snoring events, subjective daytime sleepiness and aortic root diameter in patients with and without OSA. For comparison of frequencies, \( \chi^2 \) test of independence was used. Pearson’s correlation analysis and multiple linear regression analysis were used to evaluate the relationships between the apnoea index (AI), AHI, ODI, anthropometrics and maximal aortic root diameter. A p value < 0.05 was considered to be statistically significant.
Results

Study profile and participants characteristics

Figure 1 shows the study profile. Sixty-one patients with Ghent-criteria positive Marfan’s syndrome and 26 controls completed the study protocol. Patients with Marfan’s syndrome were recruited from 41 unrelated families (no apparent relationships in their pedigree) of which 32 families provided one patient and 9 families provided two or multiple patients (mostly first degree relatives). The two groups were similar (no statistically significant difference) regarding age, gender distribution, height, weight, BMI, blood pressure and heart rate (Table 1).

Table 1. Participant’s characteristics

<table>
<thead>
<tr>
<th></th>
<th>Marfan’s N=61</th>
<th>Controls N=26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>38.3 (12.9)</td>
<td>37.2 (9.8)</td>
</tr>
<tr>
<td>Females/males</td>
<td>37/24</td>
<td>14/12</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.80 (0.11)</td>
<td>1.80 (0.10)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81.4 (20.5)</td>
<td>78.1 (15.0)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.1 (5.9)</td>
<td>24.0 (4.3)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>123.7 (14.2)</td>
<td>118.8 (11.9)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>76.2 (11.0)</td>
<td>74.4 (9.8)</td>
</tr>
<tr>
<td>Heart rate (min⁻¹)</td>
<td>62.5 (9.9)</td>
<td>65.0 (9.8)</td>
</tr>
</tbody>
</table>

Where applicable values are means (SD). BMI=body mass index; BP=blood pressure.

Patients with Marfan’s syndrome were not different from control subjects regarding neck circumference, crico-mental distance, dental overbite, Mallampati- and tonsillar size score, and retrognathic face profile, but palatal height was
significantly greater and maxillar/mandibular intermolar distance was significantly smaller in patients with Marfan’s syndrome (table 2).

Table 2. Head and neck anthropometrics

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Marfan’s N=61</th>
<th>Controls N=26</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck circumference (cm)</td>
<td>36.5 (3.6)</td>
<td>36.6 (4.2)</td>
<td>0.85</td>
</tr>
<tr>
<td>Crico-mental distance (cm)</td>
<td>7.7 (1.2)</td>
<td>8.1 (0.9)</td>
<td>0.078</td>
</tr>
<tr>
<td>Dental overbite (mm)</td>
<td>3.5 (2.7)</td>
<td>3.9 (1.7)</td>
<td>0.48</td>
</tr>
<tr>
<td>Palatal height (cm)</td>
<td>4.0 (0.7)</td>
<td>3.7 (0.7)</td>
<td>0.029</td>
</tr>
<tr>
<td>Maxillar intermolar distance (cm)</td>
<td>3.1 (0.4)</td>
<td>3.5 (0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mandibular intermolar distance (cm)</td>
<td>2.9 (0.4)</td>
<td>3.6 (0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>% retrognathic</td>
<td>21.3</td>
<td>15.4</td>
<td>0.26</td>
</tr>
<tr>
<td>Mallampati classes (%)*</td>
<td>30/44/18/8</td>
<td>38/50/12/0</td>
<td>0.36</td>
</tr>
<tr>
<td>Tonsillar size classes (%)*</td>
<td>8/74/11/7</td>
<td>0/77/19/4</td>
<td>0.36</td>
</tr>
</tbody>
</table>

Where applicable values are means (SD). * Percentage of subjects in each of the four classes (I/II/III/IV).

Sleep study, subjective sleepiness and predictors of OSA

Sleep study and subjective sleepiness

AHI and ODI were significantly higher in patients with Marfan’s syndrome compared to control subjects (table 3). Twenty patients with Marfan’s syndrome (9 females) had an AHI >5 compared to 3 subjects in the control group (one female). Eleven patients with Marfan’s syndrome had an AHI >15 compared to none in the control group. 18 patients with Marfan’s syndrome had an ODI >5 compared to only one patient in the control group (table 3, figure 2). Inspection of the data showed that the 20 cases with an AHI >5 were distributed across 16 of the 41 families.
As expected, Marfan’s patients with an AHI>5 had more snoring events/h (83.0 (94.8)) than patients with an AHI<5 (28.9 (49.1)) indicating that apnoeas were of the obstructive type (mean difference 54.1 events, 95% CI 17.4 to 90.8 events, p=0.006).

Subjective daytime sleepiness assessed by the ESS was higher in patients with Marfan’s syndrome compared to controls (table 3). Patients with an AHI >5 did not have a higher ESS (7.6 (4.3)) than patients with an AHI <5 (7.9 (5.5)) (mean difference -0.3, 95% CI -3.1 to +2.5, p=0.83).

Table 3. Sleep study and subjective sleepiness.

<table>
<thead>
<tr>
<th></th>
<th>Marfan’s N=61</th>
<th>Controls N=26</th>
<th>Difference</th>
<th>95% CI of difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI</td>
<td>5.5 (0.9-13.9)</td>
<td>3.0 (1.5-5.2)</td>
<td>+0.37</td>
<td>0.003 – 1.37</td>
<td>0.03</td>
</tr>
<tr>
<td>% patients with AHI &gt;5</td>
<td>32.8</td>
<td>11.5</td>
<td>+21.3</td>
<td>4.2 – 38.3</td>
<td>0.04</td>
</tr>
<tr>
<td>% patients with AHI &gt;15</td>
<td>18.0</td>
<td>0</td>
<td>+18.0</td>
<td>8.4 – 27.7</td>
<td>0.02</td>
</tr>
<tr>
<td>ODI</td>
<td>3.2 (0.3-9.1)</td>
<td>1.3 (0.1-3.8)</td>
<td>+0.41</td>
<td>0.01 – 1.37</td>
<td>0.02</td>
</tr>
<tr>
<td>% patients with ODI &gt;5</td>
<td>29.5</td>
<td>3.9</td>
<td>+25.7</td>
<td>12.0 – 39.3</td>
<td>0.008</td>
</tr>
<tr>
<td>ESS</td>
<td>7.8 (5.1)</td>
<td>4.6 (3.2)</td>
<td>+3.2</td>
<td>1.1 – 5.4</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Values for AHI and ODI are mean and 1 SD range (via square root transformation, and back-transformation, to normalise the distribution). Values for ESS are mean (SD). AHI=apnoea/hypopnoea index; ODI=oxygen desaturation index; ESS=Epworth sleepiness Scale. Due to displacement of the nasal cannulae, AHI could not be calculated in two patients with Marfan’s syndrome; the ODI was <5 in both subjects.

Predictors of OSA

There was a significant correlation between AHI and age (r=0.37, p=0.004), BMI (r=0.54, p=0.00001) and neck circumference (r=0.45, p=0.0004) in patients with Marfan’s syndrome. In a multiple linear regression model 33% of the variation in AHI could be explained by these factors (r²=0.33, p<0.0001), although only BMI appeared to be an independent predictor of AHI.
ODI was significantly correlated with age (r=0.44, p=0.0004), BMI (0.70, 
p<0.0001) and neck circumference (r=0.43, p=0.0007). In a multiple linear regression
model 54% of the variation in ODI could be explained by these factors (r²=0.54, 
p<0.0001), again only BMI was an independent predictor of ODI.

**Aortic root diameter**

Of the 61 patients with Marfan’s syndrome, 12 patients (19.7%) had
previously undergone surgery for aortic root dilatation. In non-operated patients,
mean aortic root diameter was significantly higher in subjects with an AHI >5 (n=16, 
4.5 (0.6) cm) than in subjects with an AHI <5 (n=32, 3.7 (0.6) cm) (mean difference 
+0.8cm, 95% CI 0.4 to 1.2 cm, p<0.0001). Percent predicted aortic root diameter 
(corrected for age and body surface area) was higher in patients with AHI>5 (127.8 
(19.3) %) than in patients with AHI<5 (116.8 (15.9) %) (mean difference 11 %, 95%
CI 0.6 to 21.5 %, p=0.039).

In non-operated patients, aortic root diameter was strongly correlated with AI 
and AHI (r=0.50, 95% CI 0.26 to 0.69, p=0.0003 for both correlations) (figure 3), and
as expected with body surface area (r=0.47, 95% CI 0.22 to 0.66, p=0.0007) and age 
(r=0.40, 95% CI 0.13 to 0.61, p=0.005). When aortic root diameter was expressed as 
% predicted, it was still significantly correlated with AI (r=0.32, 95% CI 0.04 to 0.55, 
p=0.028), whereas the correlation with AHI (r=0.27, 95% CI -0.01 to 0.51, p=0.068) 
did not quite attain statistical significance.
Discussion

This is the first case-control study on the prevalence of obstructive sleep apnoea in patients with Marfan’s syndrome showing a considerably higher frequency of obstructive sleep apnoea in patients with Marfan’s syndrome compared to matched control subjects using either a threshold for AHI of >5 or >15. This is also the first study providing data on the relationship between obstructive sleep apnoea and aortic root dilatation in patients with Marfan’s syndrome. We have found an association between the severity of obstructive sleep apnoea and the diameter of the aortic root which suggests that obstructive sleep apnoea may be a risk factor for aortic root dilatation in patients with Marfan’s syndrome.

In this study, we found that approximately 30% of all patients with Marfan’s syndrome had an AHI and ODI of >5 which is a considerably higher prevalence of OSA than in our matched controls (3.9% had an ODI>5) or in a UK population based epidemiological study (5% had an ODI>5). [20] However, Cistulli and co-workers [7] reported that 16 of 25 patients (64%) with Marfan’s syndrome had OSA (defined as AHI>5). A possible explanation for the very high prevalence of OSA found in the latter study may be a selection bias due to the relatively small number of randomly recruited patients, whereas we screened all patients attending the Oxford Marfan’s clinic for eligibility and invited every patient with Ghent-positive Marfan’s syndrome to take part in the study. Another contributory explanation may be the higher percentage of females in our study (60% compared to 52% in the study by Cistulli et al. [7]) as the prevalence of OSA is known to be lower in women than in men. [21] In the only other study on the prevalence of sleep disorders in Marfan’s syndrome, Verbraecken et al. [22] found that 4 of 15 patients (27%) had features and symptoms of sleep apnoea, although this study was based on questionnaires only.
A high frequency of craniofacial abnormalities and an increased upper airway collapsibility, resulting from the abnormally lax connective tissue, have previously been suggested as possible underlying causes for the high prevalence of OSA found in patients with Marfan’s syndrome. [6,23] In contrast to an earlier uncontrolled study in 15 patients with Marfan’s syndrome [23], we found that patients with Marfan’s syndrome were not different from control subjects regarding the frequency of a retrognathic facial profile, mean neck circumference, crico-mental distance or Mallampati score, all of which are clinical features well known to be associated with OSA. [24,25] The shorter inter-molar distance and the greater palatal height we found in patients with Marfan’s syndrome in comparison to control subjects are unlikely to contribute to the pathogenesis of OSA as there was no correlation between these measures and OSA severity, assessed by AHI, in our cohort (data not shown). Therefore, it seems that the higher prevalence of OSA found in patients with Marfan’s syndrome is more likely to be the result of an increased upper airway collapsibility rather than of craniofacial abnormalities.

The high prevalence of OSA in Marfan’s syndrome raises the question of how should an individual be assessed for potential OSA. We identified BMI as the only independent predictor of OSA in patients with Marfan’s syndrome and unexpectedly the degree of subjective sleepiness was not related to the severity of OSA. This suggests that simply assessing a patients’ subjective sleepiness is not a useful method to screen for OSA in a cohort of Marfan’s patients. Therefore, a detailed medical history including questions on snoring, apnoeas and sleepiness together with an assessment of the BMI is warranted in every patient with Marfan’s syndrome and may help the clinician to decide whether a sleep study should be performed.
Aortic root dilatation and subsequent dissection are the most life-threatening manifestations of Marfan’s syndrome. Dilatation of the aortic root can begin in childhood or early adulthood and increases at an unpredictable rate. [4,5] It is still a matter of debate which factors contribute to a rapid progression of aortic root dilatation. This is the first study in which the potential relationship between OSA and aortic root dilatation in patients with Marfan’s syndrome has been investigated. Our data show that the severity of OSA is associated with an increased aortic root diameter (figure 3), and patients with OSA had a larger aortic root than patients without OSA. These results are corroborated by the findings of two case reports in which treatment of OSA with continuous positive airway pressure (CPAP) was associated with attenuation of aortic root dilatation in three patients with Marfan’s syndrome. [8,9] This suggests that OSA promotes aortic dilatation in patients with Marfan’s syndrome. To date, the underlying mechanisms through which OSA may promote aortic dilatation in these patients are not clear. OSA has been shown to be associated with increased diurnal blood pressure as well as with recurrent surges in blood pressure during apnoeic events [26], which is the main risk factor for aortic dilatation and dissection. [27] In addition, obstructive apnoeas are associated with repeated inspiratory effort against the collapsed upper airway causing recurrent large subatmospheric intrathoracic pressures swings (sometimes over 60 mmHg) and thereby producing extensive shear stresses on intrathoracic structures including the ascending aorta. [28] This hypothesis is supported by the findings of Peters et al. who reported increased aortic diameters during obstructive apnoeas in an animal model. [29,30] Furthermore, Sampol and co-workers [31] recently found that (non-Marfan’s) patients with dissection of the thoracic aorta had a higher apnoea/hypopnoea index versus well matched hypertensive control subjects without dissection (28±30 vs
11±10, p=0.03). However, a randomized controlled trial on the effects of CPAP on aortic root diameter in patients with OSA and Marfan’s syndrome is required to prove if treatment of OSA indeed attenuates the progression of aortic dilatation.

In conclusion, we have shown that obstructive sleep apnoea is highly prevalent in patients with Marfan’s syndrome. It is not possible to reliably predict the presence of obstructive sleep apnoea in these patients by assessment of subjective sleepiness or facial morphologic features. Obstructive sleep apnoea may be a risk factor for aortic dilatation in patients with Marfan’s syndrome, and randomized controlled trials investigating the effects of continuous positive airway pressure on aortic dilatation are warranted to definitely prove this relationship.

**Competing interests**

None of the authors has a competing interest.

**Funding**

Malcolm Kohler is a recipient of a European Respiratory Society (No 118) and University of Zurich, Switzerland, research fellowship.
References


Figure legends

Figure 1: Study profile.

Figure 2: Apnoea/hypopnoea index (panel A) and oxygen desaturation index (panel B) in patients with Marfan’s syndrome (black circles) and controls (open circles). Significantly more patients with Marfan’s syndrome compared to the control group had an apnoea/hypopnoea index of >5 (32.8% vs 11.3%, p=0.04) and >15 (18.0% vs 0%, p=0.02); and an ODI >5 (29.5% vs 3.9%, p=0.008).

Figure 3: In patients with Marfan’s syndrome the apnoea/hypopnoea index showed a strong relationship with the diameter of the aortic root (r=0.50, 95% CI 0.26 to 0.69, p=0.0003). The solid line represents the regression line according to the function: aortic root diameter = 3.66+0.36*apnoea/hypopnoea index.
231 patients with possible Marfan’s syndrome screened

83 patients fulfilling Ghent criteria

- 19 did not enter the study
- 12 did not attend clinic
- 7 did not consent

64 patients with Marfan’s syndrome entered study

3 patients withdrew and had no sleep study

26 healthy controls entered study

61 patients with Marfan’s syndrome and 26 controls completed study

Kohler et al. Fig.1
A
Apnoea/hypopnoea index (events/h)

B
Oxygen desaturation index (events/h)

Kohler et al. Fig. 2
Kohler et al. Fig.3

Correlation: $r = .49494$

Aortic root diameter (cm)

Apnoea/hypopnoea index (events/h)