

# Natural evolution of moderate sleep apnoea syndrome: significant progression over a mean of 17 months

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## Abstract

**Background** – Obstructive sleep apnoea (OSA) is associated with increased morbidity and mortality. It has remained unclear whether or not it is progressive. The evolution of OSA was examined in a retrospective case note study of 55 unselected patients of mean (SD) age 55.8 (10) years with mild to moderate disease untreated by interventional methods such as continuous positive airway pressure (CPAP) or surgery. Correlations between clinical and functional variables, upper airway anatomy, and change in disease severity were also investigated.

**Methods** – Patients underwent full polysomnography on two occasions (T0 and Tx) at a mean interval of 77 (50) weeks (range 17–229). In addition, upper airway imaging with computed tomographic scanning or cephalometry had been performed in 43 patients at T0. Morbidity before, during, and after the study period was assessed by questionnaire, as was smoking history and alcohol and sedative intake.

**Results** – The apnoea hypopnoea index (AHI) for the group as a whole increased from 21.8 (11.5) to 33.4 (21.3) ( $p = 0.0001$ ). Using a 25% change in AHI to divide patients into worsened, stable, and improved groups showed that, although most of the patients deteriorated, 25 patients improved or remained stable. The change in AHI was not correlated with body mass index which remained stable at 29.7 (5.4)  $\text{kg/m}^2$  versus 29.7 (5.6)  $\text{kg/m}^2$ . There was a trend for apnoea duration to increase. No patient reported increased alcohol consumption and only one patient reported increased use of sedatives between T0 and Tx. No correlation was found between change in AHI and age, time between recordings, anatomical measurements of the upper airway, respiratory function, oximetry, or arterial blood gas tensions. Total cardiovascular and cerebrovascular morbidity was high: hypertension (26 patients, 46%), cardiac arrhythmia (17 patients, 33%), angina (12 patients, 23%), myocardial infarction (10 patients, 19%), and stroke (10 patients, 19%). Twenty nine patients (52%) were prescribed CPAP after Tx, two of whom went on to have maxillofacial surgery. These 29 treated patients had significantly higher values of AHI at

T0 and Tx and greater change in AHI than the untreated patients.

**Conclusions** – This study shows that mild to moderate OSA has a tendency to worsen in the absence of significant weight gain and that upper airway anatomy and clinical variables do not appear to be useful in predicting progression. It follows that mild to moderate OSA justifies systematic follow up. Deterioration in AHI over a mean of 17 months led to interventional treatment in over 50% of patients in the study.

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Keywords: obstructive sleep apnoea, evolution, upper airway imaging, morbidity.

Obstructive sleep apnoea (OSA) is characterised by recurrent collapse of the pharyngeal airway during sleep resulting in snoring and daytime sleepiness. It affects 4% of men and 2% of women between the ages of 30 and 60.<sup>1</sup> OSA has important pathological consequences with an increased incidence of hypertension,<sup>2,3</sup> arrhythmias,<sup>4,5</sup> myocardial infarction,<sup>6</sup> and stroke.<sup>7,8</sup> Mortality is raised,<sup>9</sup> probably largely secondary to cardiovascular causes.<sup>10</sup>

It is unclear whether or not OSA is a progressive disease. It has been proposed that snoring is a precursor to the development of OSA and that the latter itself becomes increasingly severe. This theory is supported by retrospective studies of symptoms in which patients report snoring more loudly over the years before developing nocturnal respiratory pauses which become increasingly frequent.<sup>11</sup> More recently the upper airway resistance syndrome has been described in which snoring alone in the absence of apnoeas produces sleep disruption and daytime sleepiness,<sup>12</sup> but whether or not this is a precursor to OSA remains unknown. Attempts to confirm the theory that OSA worsens with time using polysomnography have produced conflicting results. Svanborg *et al*<sup>13</sup> studied 42 patients using screening oximetry followed after at least six months by polysomnography and found that 62% of patients increased the number of desaturations per hour by 50%. However, Sforza *et al*<sup>14</sup> found no significant change in AHI (apnoea hypopnoea index) in 32 patients who underwent polysomnography on two occasions five years apart.

If OSA is indeed progressive as postulated, there are important consequences relating to

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patient treatment and follow up. Firstly, patients who have mild disease when first seen cannot be discharged as they may go on to develop more severe disease. This is particularly important in view of the fact that apnoea severity is positively correlated with complication rates, at least in the case of hypertension.<sup>15</sup> Secondly, although patients often suffer side effects with continuous positive airway pressure treatment (CPAP),<sup>16</sup> the progressive nature of the disease would make perseverance with treatment imperative. Thirdly, there may be a case for lowering the treatment threshold, particularly if it is subsequently found that adequate treatment prevents progression.

The present study was designed to examine the natural evolution of OSA and, further, if progression was found, to determine whether there are any clinical variables or anatomical characteristics of the upper airway which can predict which patients would deteriorate. We have carried out a retrospective study of 55 patients with mild to moderate OSA who had full polysomnography on two occasions at least four months (17 weeks) apart. No intervening treatment was given except advice concerning weight loss and reduction in alcohol intake if indicated. Upper airway imaging by computed tomographic (CT) scanning was carried out in 43 of these patients, 32 of whom also had cephalometry.

## Methods

### PATIENT SELECTION AND ASSESSMENT

This was a retrospective case note study. Patients had undergone polysomnography on the first occasion (T0) for investigation of symptoms suggestive of OSA. These patients had follow up polysomnography arranged routinely a minimum of 17 weeks after the initial recording without intervening treatment. Patients included in follow up were either those with mild OSA who were directed to make lifestyle changes before being reassessed as to their need for invasive treatment, or those with more severe OSA who refused invasive treatment at T0. There was no suspicion of disease progression at the outset and no financial incentive for patients to remain within the study.

Patient symptoms, in particular whether they were somnolent whilst driving, reading, watching television, whether they snored all or certain nights, and if their family had noted respiratory pauses, were assessed from the clinical case notes. Morbidity before, during, and after the study period – including cardiac arrhythmia, angina, myocardial infarction, cerebrovascular accident, and hypertension – was assessed by questionnaire, as was smoking history and alcohol and sedative intake. Arterial blood gas tensions and respiratory function tests were obtained at the first consultation and anthropometric data at the time of each polysomnographic recording.

### POLYSOMNOGRAPHY

Continuous recordings were taken of the electroencephalogram with electrode positions C3/

A2-C4/A1-Cz/O1 of the International 10–20 Electrode Placement System, eye movements, chin electromyogram, and electrocardiogram with modified V2 lead. Respiration was monitored with uncalibrated inductance respiratory plethysmography. Airflow was measured by the sum of buccal and nasal thermistor signals and oxygen saturation was measured with a Biox-Ohmeda 3700 oximeter.

The polysomnogram was scored manually according to standard criteria.<sup>17</sup> Episodes of apnoea were defined as complete cessation of airflow for 10 seconds or more and hypopnoea as a decrease of more than 50% in oronasal airflow lasting for at least 10 seconds. Apnoea/hypopnoea events were classified as central, obstructive, or mixed according to the absence or presence of breathing efforts. The variation in oxygen saturation overnight was quantified as the Delta index calculated by the method validated by Levy *et al.*<sup>18</sup>

### UPPER AIRWAY IMAGING

#### Cephalometry

Lateral cephalometric radiographs were obtained using the technique described by Riley *et al.*<sup>19</sup> The following measurements were made from the radiographs:

(a) MP-H: the distance from the mandibular plane to the hyoid bone.

(b) PAS: the posterior airway space measured between the posterior pharyngeal wall and the dorsum of the tongue.

(c) PNS-P: the distance from the posterior nasal spine to the tip of the palate (soft palate length).

(d) W: the maximal width of the soft palate.

(e) DR: the angle between the line joining the nasion to the anterior nasal spine and the line joining the nasion to the supramentale (an indication of the degree of retrognathism).

#### Computed tomographic (CT) scanning

The purpose of CT scanning was to measure the luminal area of the airway at the level of the nasopharynx, oropharynx, and hypopharynx and the width of the base of the tongue. The subjects were placed in the supine position on the scanning table with the neck placed in a neutral position midway between flexion and extension. Eight to ten slices 5 mm thick were imaged every 10 mm from the hard palate to the upper limit of the epiglottis. All scans were perpendicular to the airway. The luminal area was measured with an integral software program using the exact contours of the pharyngeal lumen.

### DATA ANALYSIS

Comparison of variables from the first polysomnographic recording (T0) with those of the second (Tx) was made using the ANOVA test. To examine the possibility of a relationship between change in AHI and clinical variables a correlation matrix was constructed of ratio change in AHI (AHI Tx/AHI T0) as the independent variable against body mass index

Table 1 Mean (SD) and ranges for patient age, arterial blood gas tensions, respiratory function, and upper airway anatomical measurements at T0

	Mean (SD)	Range	Normal values
Age (years)	55.8 (9.7)	19–72	
PaO <sub>2</sub> (mm Hg)	76.0 (9.7)	55–97	
Paco <sub>2</sub> (mm Hg)	39.5 (3.5)	31–45	
Sao <sub>2</sub> (%)	94.7 (1.9)	89–98	
FEV <sub>1</sub> (l)/% predicted	3.0 (0.85)/96 (21)	1.27–4.54/44–132	
FEV <sub>1</sub> /VC (%)	81 (9)	55–98	
PNS-P (mm)	38.5 (4.8)	30–48	34.0 (6.0)*
PAS (mm)	11.2 (4.4)	3–22	11.0 (2.0)*
MPH (mm)	19.4 (7.02)	8–33	15.4 (3.0)*
W (mm)	10.2 (2.1)	6–14	10.2 (2.1)†
DR (°)	3.2 (2.1)	0–9	<2
Tongue width (mm)	48.5 (5.1)	40–60	47 (4)§
Rhinopharynx area (mm <sup>2</sup> )	427.0 (115.0)	201–699	540 (130)¶
Oropharynx area (mm <sup>2</sup> )	96.0 (52.2)	43–293	260 (90)¶
Hypopharynx area (mm <sup>2</sup> )	208.0 (82.0)	53–400	340 (160)¶

PaO<sub>2</sub>, Paco<sub>2</sub> = arterial oxygen and carbon dioxide tensions; Sao<sub>2</sub> = oxygen saturation; FEV<sub>1</sub> = forced expiratory volume in one second; VC = vital capacity. Anatomical measurements defined in text.

Normal values of upper airways measurements from: \* Jamieson *et al. Sleep* 1986;9:469–77; † Strelzow *et al. Laryngoscope* 1988; 98:1149–58; ¶ Haponik *et al. Am Rev Respir Dis* 1983; 127:221–6; § Larsson *et al. Acta Radiol* 1988;29:401–5.

Table 2 Mean (SD) values at T0 and Tx for body mass index (BMI), polysomnography, oximetry, cigarette and alcohol consumption

	T0	Tx
BMI (kg/m <sup>2</sup> )	29.7 (5.4)	29.6 (5.6)
AHI (events/hour)	21.8 (11.5)	33.4 (21.3)**
Mean apnoea duration (sec)	17.6 (3.9)	19.0 (6.3)
Mean hypopnoea duration (sec)	19.4 (5.8)	19.0 (4.8)
Delta index	0.87 (0.48)	1.13 (1.07)
Mean Sao <sub>2</sub> (%)	92.5 (2.4)	92.7 (4.0)
Minimum Sao <sub>2</sub> (%)	77.5 (10.2)	76.6 (15.9)
Time <90% Sao <sub>2</sub> (min)	70.1 (101.3)	57.2 (81.1)
Total sleep time (min)	410.2 (98.3)	381.6 (88.4)*
%REM sleep	10.0 (6.6)	12.8 (7.0)*
% Stage 1	21.6 (20.9)	18.5 (11.9)
% Stage 2	64.4 (22.2)	59.7 (19.9)
% Stage 3 and 4	2.1 (4.0)	2.7 (3.7)
Cigarettes per day	2.8 (9.6)	2.9 (10.5)
Cigarette pack/years	13.8 (17.1)	14.2 (17.9)
Alcohol units per day	1.3 (1.6)	1.1 (1.5)

\* p < 0.05; \*\* p = 0.0001.

(BMI), age, time between the two recordings (Tx – T0), rhinopharyngeal area, oropharyngeal area, hypopharyngeal area, tongue base width, posterior airway space (PAS), hyoid bone position (MPH), degree of retrognathia (DR), soft palate width (W) and length (PNS-P), and blood gas and lung function test values. There was no prior hypothesis that any one particular variable would influence disease pro-

gression. Comparison of clinical variables between the groups of patients who improved, worsened, or stayed the same (using increases or decreases in AHI at Tx of 25% and 50% compared with T0 to define worsened and improved groups, respectively) was carried out using the Kruskal-Wallis test.

## Results

The mean (SD) and ranges at T0 of patient age, respiratory function measurements, arterial blood gas tensions, and upper airway anatomical values are shown in table 1. As a group the patients had normal blood gas tensions and respiratory function. The upper airway dimensions were in keeping with those found in previous studies of patients with OSA.<sup>20–23</sup>

Figure 1 shows a comparison of BMI, AHI, AI (apnoea index), and HI (hypopnoea index) at T0 and Tx where Tx was a mean (SD) of 77 (50) weeks after T0 (range 17–229). A significant increase in AHI was seen from 21.8 (11.5)/h to 33.4 (21.3)/h (p = 0.0001). There were also significant increases in AI and HI. However, BMI remained unchanged.

Table 2 lists mean variables at T0 and Tx including AHI, BMI, polysomnographic data, and cigarette and alcohol consumption. The duration of hypopnoea, mean and minimum overnight oxygen saturations, and the percentage of time spent in each phase of non-

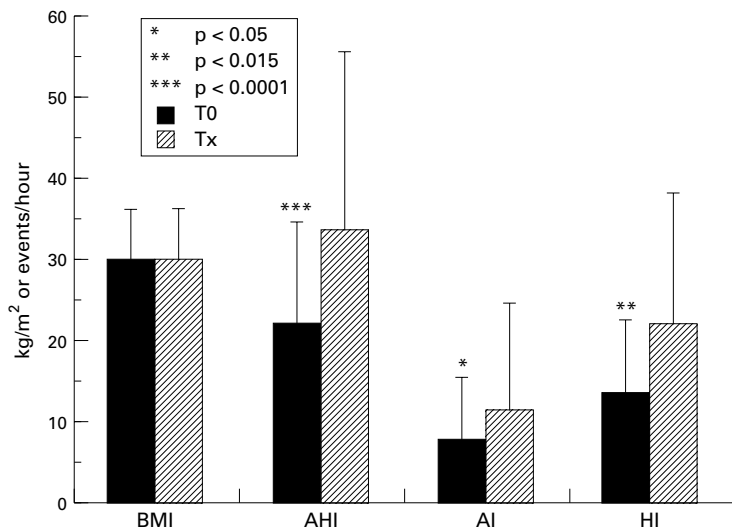


Figure 1 Body mass index (BMI), apnoea hypopnoea index (AHI), apnoea index (AI), and hypopnoea index (HI) at T0 and Tx.

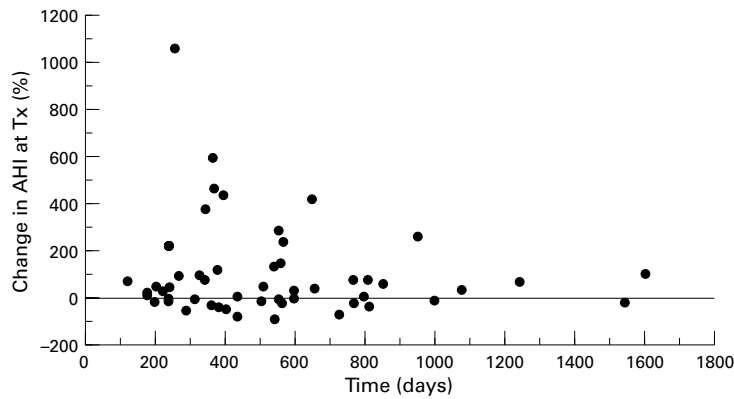


Figure 2 Scatter plot of percentage change in apnoea hypopnoea index (AHI) against time between recordings (T0 - Tx).

REM sleep did not change significantly. Total sleep time was reduced whilst mean apnoea time and delta index both showed non-significant upward trends. Alcohol and cigarette consumption remained stable.

Figure 2 is a scatter plot of ratio change in AHI (AHI Tx - AHI T0/AHI T0) against time between recordings (Tx - T0). There was no correlation between the two variables.

Comparisons of AHI, AI, HI, BMI and age between men (n = 47) and women (n = 8) at T0 revealed no significant difference. Both sexes showed an increase in AHI at Tx compared with T0. This was less marked and non-significant in women (22.2 (11.6) versus 35.3 (22.0) (p = 0.0001) in men compared with 19.7 (11.1) versus 22.6 (12.1) (p = NS) in women).

Table 3 compares groups of patients who improved, worsened, or stayed the same. A 25% increase or decrease in AHI at Tx compared with T0 was used to select worsened or improved patients, respectively, the remaining patients being classed as stable. Thirty patients deteriorated whilst 25 patients improved or remained stable. No significant difference between worsened, improved, and stable groups in terms of age, BMI, Tx - T0 time, or upper airway anatomy was found (it should be noted that only three patients in the improved group had upper airway imaging). However, both worsened and improved groups showed a trend

towards a lower AHI at T0 at 19.7 (11.4) and 21.6 (10.8) respectively when compared with the stable group at 26.1 (11.5). Using a ratio change of 50% as the cut off point gave similar results. There was a non-significant trend towards increased morbidity in the worsened group (p = 0.068).

The correlation matrix constructed with percentage change in AHI ( $\Delta$ AHI) as the fixed variable showed no correlation with age, time between recordings (Tx - T0), upper airway anatomical values, BMI, blood gas tensions, or respiratory function.

The smoking habits and use of alcohol and sedatives of the patients between T0 and Tx remained unchanged in the majority of patients (38 of 55). No patient reported increased alcohol consumption, one patient reported increased tobacco intake, and one patient took more sedatives. Most of the changes which did occur constituted reductions or cessations. Patient symptoms showed no change in snoring or daytime sleepiness between T0 and Tx.

Concerning the incidence of morbidity, data on hypertension were available for all 55 patients whereas 52 of the 55 patients responded to the questions on myocardial infarction, angina and stroke and 51 patients (the four non-responders being the previous three plus one other) responded to the question on arrhythmia. Figure 3 shows the number of patients who suffered cardiovascular or cerebrovascular events over their life times up to the point of receipt of the questionnaire as a fraction of the total number of patients responding to the questionnaire as follows: hypertension, 26 of 55 (46%); cardiac arrhythmia, 17 of 51 (33%); angina, 12 of 52 (23%); myocardial infarction, 10 of 52 (19%), stroke, 10 of 52 (19%).

It should be noted that the patients in the group who reported events were significantly older than those in the group who did not at 57 (7) years and 53 (12) years, respectively (p = 0.0163).

Looking in particular at the period between T0 and Tx (77 (50) weeks) revealed that over this time four patients manifested cardiovascular disease (fig 3). Between Tx and the date of the questionnaire (71 (49) weeks, range 4-186), six patients suffered cardiovascular or

Table 3 Mean (SD) values at T0 of BMI, AHI, AI, HI, T0-Tx interval and upper airway anatomy between worsened, improved and stable groups using a 25% change in AHI as the cut off point (upper airway measurements were performed on 43 of the 55 patients and only three of the nine patients in the improved group)

	Worsened (n = 30)	Improved (n = 9)	Stable (n = 16)
Time interval T0-Tx (days)	540 (344)	526 (196)	484 (373)
Age (years)	56.5 (7.5)	49.7 (15.7)	57.4 (8.7)
BMI (kg/m <sup>2</sup> )	30.4 (5.1)	27.8 (5.7)	29.2 (5.8)
AHI (events/hour)	19.7 (11.4)	21.6 (10.8)	26.1 (11.5)
HI (events/hour)	12.6 (7.3)	12.9 (7.6)	15.1 (9.5)
AI (events/hour)	5.9 (6.4)	8.7 (4.5)	10.4 (7.8)*
PNS-P (mm)	38.3 (3.9)	39.3 (6.6)	38.7 (6.0)
PAS (mm)	12.2 (4.7)	8.3 (3.1)	10.4 (3.9)
MPH (mm)	19.3 (5.8)	14.5 (6.4)	21.4 (8.9)
W (mm)	10.1 (2.1)	10.3 (2.8)	10.6 (2.1)
Tongue width (mm)	49.1 (5.8)	49.0 (2.0)	47.6 (4.4)
Rhinopharynx area (mm <sup>2</sup> )	445 (124)	451 (194)	390 (81)
Oropharynx area (mm <sup>2</sup> )	96 (48)	71 (15)	104 (66)
Hypopharynx area (mm <sup>2</sup> )	209 (92)	200 (82)	199 (63)

BMI = body mass index; AHI = apnoea hypopnoea index; HI = hypopnoea index; AI = apnoea index. Anatomical measurements defined in text.

\* p<0.05.

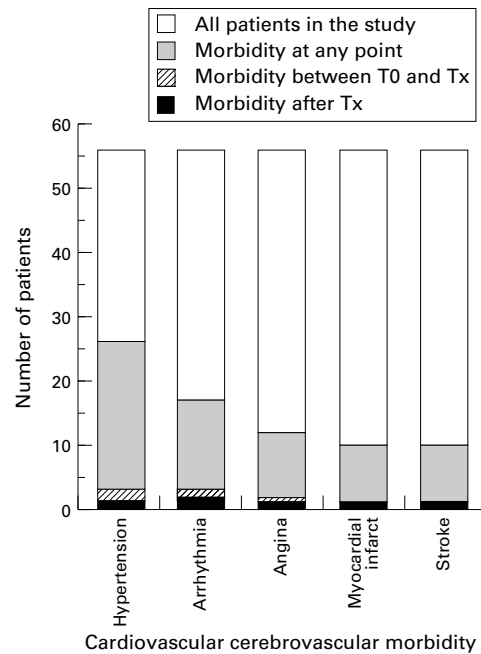


Figure 3 Cardiovascular and cerebrovascular morbidity (before T0, between T0 and Tx, and after Tx up until the time of the questionnaire) as a fraction of the total number of patients in the study.

cerebrovascular events of whom four were receiving CPAP treatment. One of these six patients who suffered a myocardial infarction was the patient who had developed angina between T0 and Tx. There was a non-significant trend towards greater age in the group comprising the nine patients who reported events after T0 compared with the patients who were event free during this period. Further, these nine patients had a significantly greater change in AHI between T0 and Tx than the remaining patients (18.2 (29.9) and 10.5 (18.1), respectively;  $p = 0.0477$ ) despite an initial AHI that was not significantly different between the two groups (21 (8.8) and 22.0 (12), respectively).

With regard to treatment after Tx, 29 patients (52%) were prescribed CPAP of whom

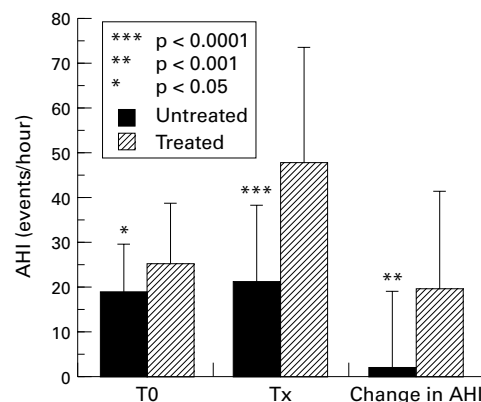


Figure 4 Comparison of apnoea hypopnoea index (AHI) at T0 and Tx and change in AHI in patients who received treatment by CPAP (treated) after Tx and those who did not (untreated).

three went on to have surgery (two maxillofacial and one palatal). Twenty six patients were felt to have improved or to be sufficiently stable not to require invasive treatment. A comparison of AHI at T0 and Tx in the treated group with the untreated group is shown in fig 4. The treated group had higher AHI values at both T0 and Tx and a greater increase in AHI.

## Discussion

Our results show that a significant increase in AHI occurred in a group of patients with mild to moderate OSA over a mean of 17 months which was not related to an increase in BMI. Using a 25% change in AHI to divide patients into worsened, stable and improved groups showed that, although most of the patients deteriorated, 25 improved or remained stable. Most of the patients did not change their alcohol and sedative consumption or cigarette smoking between the two recordings. This rise in AHI was not accompanied by a change in symptoms. We found no evidence that age, upper airway anatomical variables, respiratory function, or arterial blood gas tensions at T0 predicted which patients would progress. Twenty nine patients (52%) went on to CPAP treatment after Tx of whom three also had surgery.

Two previous studies examining the evolution of OSA using polysomnography in patients untreated by CPAP or surgery have been carried out to our knowledge. Svanborg *et al*<sup>13</sup> undertook a retrospective study of 42 patients with OSA who had undergone screening using a static charge sensitive bed and oximetry at least six months prior to a diagnostic polysomnogram. In comparing the result of the screening night with that of the follow up night, they found that 62% of the patients had increased the number of desaturations per hour by more than 50%. This was correlated to an increase in body weight. However, some patients showed considerable increase in respiratory disturbance in the absence of weight gain.

In that study the conditions on the initial and follow up nights were not identical: patients underwent oximetry and static charge sensitive bed screening on the first occasion but on the second occasion they had full polysomnography. It follows that the greater degree of respiratory disturbance seen on the second night may well have been secondary to the presence of the polysomnography apparatus rather than reflecting a progression in the patient's clinical state.

In the study by Sforza *et al*<sup>14</sup> patients with a diagnosis of OSA who had undergone polysomnography five years before but who had refused treatment underwent repeat polysomnography. The sample size was relatively small as, although 58 patients were eligible for the study, only 32 agreed to instrumental follow up. No change in AHI was found in the group as a whole, the only significant change being the increase in duration of apnoeas and hypopnoeas. Furthermore, in the group of patients who had deteriorated, BMI rose significantly

but was not significantly correlated with the change in AHI. Neither Svanborg nor Sforza obtained information about alcohol intake and the use of sleeping pills or other sedatives which could have influenced the results.

Our study could be criticised as retrospective but, since patients underwent repeat polysomnography as a routine measure rather than because they were becoming more symptomatic, there should not have been any weighting in favour of patients who got worse. In addition, the fact that patient symptoms were unchanged at Tx would suggest that there was no bias in favour of deterioration. On the other hand, all studies comparing polysomnography data suffer from the fact that there is some variability in night to night recording,<sup>22,25</sup> but we have included 55 patients in this study which should have reduced the importance of this factor.

Our results are in agreement with those of Svanborg *et al* in that we have shown a deterioration in AHI over time, in contrast to the findings of Sforza *et al*. The reason for these conflicting results may be the degree of severity of OSA in the populations studied. It is interesting to note that the mean follow up AHI for our group was similar to that of Svanborg at 35.1 and 23.5, respectively, whereas that of the group studied by Sforza, in which no deterioration was seen, was considerably higher at 52.2. This may indicate that at high levels of AHI further deterioration does not occur and, indeed, it is difficult to see how OSA could progress indefinitely.

We found no significant correlation between BMI and AHI. This was also the case in the Sforza study and, although Svanborg *et al* did find a correlation, there were some patients who developed increased respiratory disturbance in the absence of a change in BMI. Thus, it appears that factors other than an increase in BMI are important in OSA progression.

In our study comparison of groups of worsened, improved, and stable patients showed no significant differences in upper airway anatomy, respiratory function, or age. However, there was a trend towards lower AHI and AI at T0 for both improved and worsened groups compared with the stable group whether the cut off point was a change in AHI of 25% or 50%. This may be because there is a degree of unpredictability in the evolution of mild OSA in that it may either improve or worsen (with the weighting in favour of progression) but that more severe OSA does not tend to remit. Interestingly, there was no significant difference in the time between recordings in the three groups. The absence of a link between change in AHI and the time between recordings was also seen in the scatter plot of the two variables.

Having established that mild to moderate OSA shows a tendency to deteriorate, we used upper airway imaging to determine whether there were any anatomical characteristics of the upper airway which predicted which patients would get worse. Patients with OSA have been shown to have both bony abnormalities, such as a posteriorly positioned mandible and low

set hyoid bone, and soft tissue enlargement causing a narrow posterior airway space, large tongue, long soft palate, and reduction in pharyngeal diameter.<sup>22-23</sup> We found no correlation between any of these variables and change in AHI. Thus, although upper airway abnormalities predispose to the development of OSA, they do not appear to influence OSA progression and are thus not predictive of which patients will get worse. In addition, our finding that OSA deterioration occurs in the absence of an increase in BMI would argue against increased fat deposition as the cause of progression in our patients.

Functional factors have also been implicated in apnoea generation. We would postulate that OSA progression is secondary to exacerbation of such factors in the absence of evidence for anatomical mechanisms. It has been shown that pharyngeal temperature sensitivity is decreased in apnoeic patients,<sup>26</sup> presumably through sensory nerve or receptor damage, and it has been suggested that snoring induced trauma may be the cause. Pharyngeal mechanoreceptors and the nerves important in airway reflex arcs which maintain airway muscle tone<sup>27,28</sup> may be affected by the same mechanism. Progressive loss of function of these reflexes could contribute to worsening apnoea. Muscle lesions are also seen in apnoeic patients,<sup>29-31</sup> indicating damage which may be important in increasing airway collapsibility. In addition, mechanisms such as ventilatory instability and incoordination of muscle activity have been proposed which may show a tendency to worsen with time.<sup>32-34</sup>

In this study we found no significant difference in BMI, AHI, or age between men and women at T0. Both sexes showed an increase in AHI at Tx, although this was smaller and non-significant in women, but it should be noted that the sample size was small. It is established that women have a lower incidence of OSA than men and our results may suggest that, in addition, disease progression may be slower.

The assessment of patient symptoms in our study showed that there was no change in snoring or daytime sleepiness despite the increase in AHI. This may be because symptoms are known to correlate poorly with disease severity in OSA.<sup>35,36</sup> It may also be because, at the time when most of the patients studied underwent polysomnography, a validated reproducible scale for symptom scoring such as the Epworth Sleepiness Scale<sup>37</sup> was not available to us from the case notes.

The importance of establishing that OSA is a progressive disease lies largely in the fact that it is associated with increased morbidity and mortality. In our study there was a high overall incidence of hypertension and cardiovascular disease. The nine patients who developed cardiovascular problems between T0 and receipt of the questionnaire showed a significantly greater change in AHI between T0 and Tx than the other patients, despite having a similar AHI at T0, but were not significantly older. Looking at morbidity in the group of 25 worsened patients as selected by a 25% increase

in AHI showed a non-significant trend towards an increased number of events in this group compared with the stable and improved groups. Thus, our findings would seem to suggest that mild to moderate OSA is associated with a high incidence of cardiovascular disease and, furthermore, that higher rates of change of AHI may be associated with increased risk of morbidity. A prospective trial is needed to confirm our conclusions.

Most of our patients went on to CPAP after Tx – an indication that clinical deterioration had occurred in the opinion of the treating physicians or that lifestyle changes had been insufficient to produce significant improvement. Given that our results showed disease progression it could be argued that, in future, similar patients will start treatment sooner, particularly as this may reduce associated cardiovascular complications. The treatment threshold may also be lowered if it becomes clear that treatment prevents progression.

In conclusion, our study showed that mild to moderate OSA progressed in a majority of patients in the absence of weight gain and that upper airway anatomy or respiratory function was not useful in predicting which patients would get worse. The mechanism of progression of OSA may involve several functional factors such as ventilatory instability or snoring induced trauma to the upper airway.

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