

Sleep disordered breathing following stroke

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ABSTRACT: *Sleep disordered breathing following stroke. P.M. Turkington, M.W. Elliott.*

In recent years there has been increasing interest in the relationship between obstructive sleep apnoea and stroke. It is clear that many patients who have had a stroke have marked obstructive sleep apnoea. This is seen during recovery but also during the acute phase when

transient hypoxaemia and the blood pressure swings associated with upper airway obstruction, may worsen the ischaemic penumbra of the area of the brain which is compromised, leading to a worse outcome. There is some evidence to support this hypothesis. This article explores these issues.

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Introduction

Obstructive sleep apnoea (OSA) is a disorder characterised by the occurrence of repeated episodes of complete or partial pharyngeal obstruction during sleep, leading to sleep fragmentation and oxygen desaturation. Typical symptoms are of disruptive snoring and daytime hypersomnolence, however more recently OSA has been associated with a range of cardiovascular and neuropsychological sequelae. This has led to the hypotheses that OSA is a cause of systemic hypertension [1, 2, 3, 4, 5] and is a risk factor for cardiovascular disease [6, 7, 8, 9, 10] and stroke [11, 12, 13, 14, 10]. However, because of epidemiological difficulties in research investigating such relationships, this may never be formally "proved". Regardless, interest in the relationship between OSA and stroke continues to grow and in particular several studies have now reported a high prevalence following stroke [15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. Disentangling whether OSA predates and therefore is a risk factor for stroke, or whether OSA is a consequence of stroke is difficult and the issue may never be fully resolved [23, 26, 27]. Whether OSA in the immediate post stroke period predated or was caused de novo by the stroke may not matter if it has an important effect on functional outcome and recovery and is amenable to intervention. The main focus of this review will be on the prevalence of OSA following stroke, whether it can be predicted, its haemodynamic consequences, the effect it has on functional outcome and whether it can and should be treated.

Prevalence and apnoea type

Initial reports in the medical literature suggested that central sleep apnoea, and in particular Cheyne Stokes respiration (CSR), was the common form of sleep disordered breathing (SDB) following both hemispheric [28, 29, 30] and brainstem [31, 32, 33] strokes. This was thought to be due to heightened central responsiveness to carbon dioxide. However many of these studies only recorded respiratory effort using impedance pneumography without monitoring airflow and hence probably underestimated obstructive apnoeic events. The earliest report of OSA after stroke was in the form of a case report [34] in 1988. This was followed 3 years later, by work published only as an abstract, because it lacked a control group, which reported that OSA (RDI > 10) was present in 72% of patients after stroke [35]. Since then several studies (summarised in table 1) have reported a high prevalence (32-94%) of SDB following stroke and in particular have suggested that obstructive apnoea predominates [15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. Only two of these studies assessed the immediate (first 24 hour) period after stroke [21, 24] when OSA may have its greatest effect on the post stroke ischaemic penumbra, because of the changes in oxygen saturation and blood pressure which accompany an obstructive event. One study examined patients much later in the rehabilitation phase of the stroke [20] and found a lower prevalence of SDB (44%), suggesting improvement with the passage of time. Furthermore three studies [22, 23, 19] restudied patients several months after the initial sleep study;

Table 1. - Summary of studies reporting OSA following stroke. Time to start of study expressed as mean time from onset of neurological symptoms except * which are given as the range of times to when study started and ‡ which is from time of admission to hospital. Prevalence of SDB expressed as RDI>10 per hour except † which is RDI>20 per hour and § which is number of >4% desaturations per hour

Study	Number of Patients Studied	Stroke or TIA	Time to Start of Study	Type of Study	Prevalence of SDB	Percentage Predominant Obstructive Apnoea
Mohsenin	10	Stroke	Up to 12 months*	Full PSG	80%†	90%
Good	47	Stroke	15 days	Oximetry	32%§	N/A
Dyken	24	Stroke	15.7 days	Full PSG	71%	100%
Wessendorf	147	Stroke	46 days	Full PSG	44%	94%
Bassetti	80	Both	9 days	Full PSG	62.5%	94%
Parra	161	Both	24-48 hours*	Respiratory Variable only PSG	72%	61.5%
Turkington	120	Stroke	10.8 hours	Respiratory Variable only PSG	60.8%	91%
Harbison	68	Stroke	10 days	Respiratory Variable only PSG	94%	N/A
Iranzo	50	Stroke	11.6 hours	Full PSG	62%	93.5%
Kaneko	62	Stroke	6 weeks	Full PSG	72%	88%
Hui	51	Stroke	2.7 days‡	Full PSG	67%	100%

PSG = polysomnography, SDB = Sleep disordered breathing, RDI = Respiratory desaturation index.

all found that the prevalence of SDB reduced. One suggested the improvement was due to a reduction in obstructive apnoeas [22] and another suggested it was due to an improvement in central apnoea [19], however this study may not be reflective of a typical stroke population (TIA patients included and only 5% mortality at 3 months) and furthermore there was an unusually high predominance of central apnoea (38%) on the initial study. The study of Harbison et al [23] demonstrated a high RDI in the initial post stroke study (94% RDI>10) which significantly fell in the follow up studies performed 6 weeks later (mean (SD) RDI 31 (17) vs 24 (16)). Although the authors were not able to delineate the predominant type of apnoea (obstructive or central), due to sleep study equipment used, the population studied was very typical of a stroke population in terms of age and stroke severity.

Prediction of SDB post stroke

The majority of the evidence suggests that OSA type risk factors are the best predictors of SDB post stroke: Increasing body mass index has been associated with post stroke SDB in three studies [21, 20, 18], however associations with neck circumference [21, 20], snoring [20] and pre-stroke sleepiness [36] have also been demonstrated. The majority of studies [21, 18, 20, 17] have failed to show associations with stroke characteristics (severity, location, pharyngeal muscle function or clinical subtype) suggesting the patients who develop SDB post stroke are predisposed by body habitus and that SDB is not just a marker of severe stroke. Two studies have however suggested that

SDB post stroke is more severe in the lacunar syndrome [23, 36], but this clinical subtype of stroke is known to have a greater association with hypertension.

Haemodynamic consequences of SDB post stroke and its implications

Following an acute stroke areas of the brain are thought to become critically ischaemic, with areas in boundary zones and areas supplied by terminal arteries most susceptible (the so called ischaemic penumbra) and any fluctuation in cerebral blood flow or blood oxygen saturation at this time maybe critical. Up to 43% of stroke patients will have a progression of their neurological deficit [37, 38] and this typically occurs early after stroke onset with 87% occurring within the first 48 hours [39]. Iranzo et al demonstrated a link between early neurological deterioration and SDB occurring within 24 hours of stroke onset [24].

Blood pressure variability in patients with acute stroke has been shown to be significantly higher than in age and sex matched controls [40, 41] and a further study by Dawson et al [42] demonstrated that this blood pressure variability is significantly associated with a poor outcome at 30 days. This is probably due to a direct effect on cerebral blood flow, which is likely to be pressure dependent as cerebral autoregulation is diminished post stroke [43]. Furthermore, the sensitivity of the baroreceptor reflex, which is responsible for the rapid adjustment of blood pressure around the existing mean level, has been shown to be reduced after stroke [40, 41], which in turn has been

demonstrated to increase variability in blood pressure [44, 45]. Obstructive apnoea has been demonstrated in the non stroke setting to be associated with several haemodynamic fluctuations [46] and therefore may contribute to the blood pressure variability seen in the acute stroke period. However a recent study failed to demonstrate a clear association between the two [47]. The study found that more 10 mmHg and 15mmHg dips in blood pressure occurred in acute stroke (with or without SDB) patients than in age, sex and body mass index matched controls. However the acute stroke patients with SDB had almost three times more 10 & 15 mmHg dips in blood pressure than those without SDB and there was a positive correlation between the number of dips in blood pressure and the severity of SDB in the acute stroke patients. This may suggest that SDB, occurring on a background of impaired baroreceptor function may significantly contribute to increased blood pressure variability seen after stroke and because of the loss of cerebral autoregulation cause further damage to the ischaemic penumbra. This may be further compounded by repeated oxygen desaturation and disturbances in inflammatory and coagulation profiles, particularly cytokines and fibrinogen, associated with SDB.

Evidence that SDB has an effect on outcome post stroke

There is increasing evidence to suggest that SDB following acute stroke does have a deleterious effect on mortality and morbidity. Spriggs et al studied 400 patients admitted to hospital with stroke and 400 age and sex matched controls [12] and found that the six month survival rates post stroke were 79% in patients who never snored prior to the stroke, 77% in patients who occasionally snored prior to the stroke, 62% in patients who often snored prior to the stroke and 52% in patients who always snored prior to the stroke. The early (within 7 days) and late (after 7 days) mortality rates in non regular snorers (4% and 18%) were also significantly lower than in regular snorers (15% and 30%). However this study relied on self reported snoring and not on sleep studies to evaluate whether or not the patients had OSA.

Good et al reported that the post stroke oximetry variables of mean oxygen saturation, time spent less than 90% saturation, number of desaturations and desaturation index correlated with Barthel index at discharge and improvement in Barthel index from admission to discharge [16].

More recently it has been shown that upper airway obstruction occurring within the first 24 hours

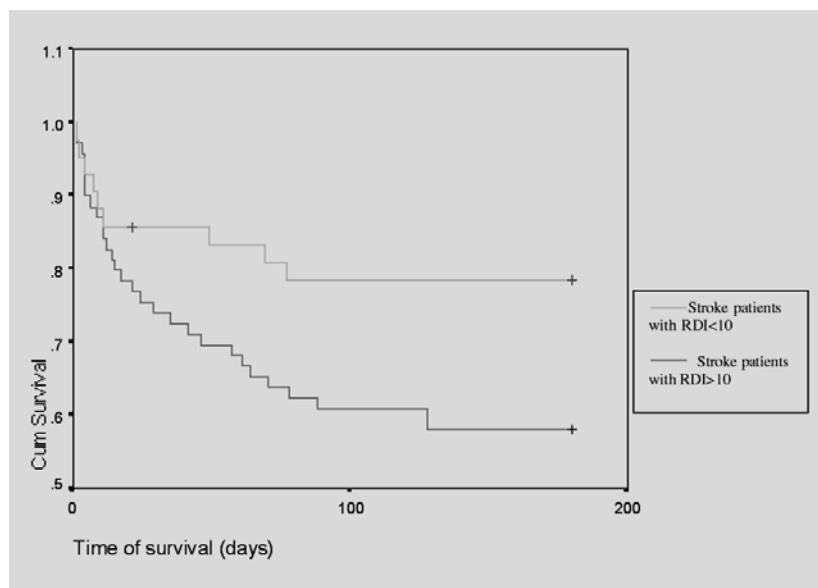


Fig. 1. - Kaplan Meier Survival Plot. Stroke patients with a RDI<10 have significantly longer survival time compared to those with an RDI>10 ($p<0.04$).

after stroke has a significant effect on outcome, increasing the likelihood of death (figure 1) and dependency at 6 months [48]. In this study stroke patients with frequent obstruction of their upper airway appeared to die sooner than those without SDB, and the surviving patients spent longer in hospital if they experienced SDB. The study also suggested that longer apnoeas and hypopnoeas and more severe desaturations had a greater deleterious effect.

Treatment of SDB post stroke

With evidence suggesting that SDB is not only common post stroke but also that it has a detrimental effect in outcome of stroke, thought has turned to its treatment. The fact that one study demonstrated higher levels of SDB when patients were in the supine or near supine positions [21] does suggest that careful positioning of patients in the immediate period after the stroke may be important. However the main focus of attention has been on CPAP, as this is well established as the gold standard treatment in OSA, but this has proved challenging with studies demonstrating poor tolerance and others suggesting possible adverse effects in the post stroke setting.

Two studies have shown CPAP compliance rates of between 50-70%, in groups of patients who were highly selected and in the stable phase following their stroke [49, 50]. Greater disability and lower levels of consciousness were associated with lower levels of compliance suggesting that effective CPAP therapy may be even more difficult in the acute phase. This has been born out by the results of a further study [22], in which only 16 of 34 patients who had significant OSA (RDI>10) at day 4 post stroke could tolerate a CPAP titration. The majority of these patients (14) refused any further CPAP after a 30 minute acclimatisation period. Furthermore only 4 patients, all of whom had

typical OSA features (snoring and daytime hypersomnolence) continued to use CPAP at home after discharge from hospital. CPAP has been demonstrated to decrease cerebral blood flow velocity (correlated to reduction in PetCO_2), in normal volunteers studied during wakefulness [51], which could be potentially harmful post stroke and possibly may even explain the poor levels of compliance seen in the other studies. Further careful studies assessing both safety and tolerance of CPAP in stroke patients, focusing on those at most risk of OSA and with the aim of abolishing more severe apnoeas and desaturations are now required. If these prove successful then a large randomised controlled trial will be needed to establish whether or not treatment of SDB post stroke has any impact in improving outcome after stroke.

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