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SLEEP APNEA RELATED RISK OF MOTOR VEHICLE ACCIDENT IS REDUCED BY CPAP

Sleep Apnea Related Risk of Motor Vehicle Accidents is Reduced by Continuous Positive Airway Pressure: Swedish Traffic Accident Registry Data

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Study Objectives: Obstructive sleep apnea (OSA) is associated with an increased risk of motor vehicle accidents (MVAs). The rate of MVAs in patients suspected of having OSA was determined and the effect of continuous positive airway pressure (CPAP) was investigated.
Design: MVA rate in patients referred for OSA was compared to the rate in the general population using data from the Swedish Traffic Accident Registry (STRADA), stratified for age and calendar year. The risk factors for MVAs, using demographic and polygraphy data, and MVA rate before and after CPAP were evaluated in the patient group.
Setting: Clinical sleep laboratory and population based control (n = 635,786).
Patients: There were 1,478 patients, male sex 70.4%, mean age 53.6 (12.8) y.
Interventions: CPAP.
Measurements and Results: The number of accidents (n = 74) among patients was compared with the expected number (n = 30) from a control population (STRADA). An increased MVA risk ratio of 2.45 was found among patients compared with controls (P < 0.001). Estimated excess accident risk was most prominent in the elderly patients (65–80 y, seven versus two MVAs). In patients, driving distance (km/y), EDS (Epworth Sleepiness score ≥ 16), short habitual sleep time (≤ 5 h/night), and use of hypnotics were associated with increased MVA risk (odds ratios 1.2, 2.1, 2.7 and 2.1, all P ≤ 0.03). CPAP use ≥ 4 h/night was associated with a reduction of MVA incidence (7.6 to 2.5 accidents/1,000 drivers/y).
Conclusions: The motor vehicle accident risk in this large cohort of unselected patients with obstructive sleep apnea suggests a need for accurate tools to identify individuals at risk. Sleep apnea severity (e.g., apnea-hypopnea index) failed to identify patients at risk.
Keywords: CPAP, daytime sleepiness, driving distance, risk factors, traffic accident
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INTRODUCTION

Sleepiness at the wheel is a major cause of motor vehicle accidents (MVAs).[1,2] Obstructive sleep apnea (OSA) is associated with excessive daytime sleepiness (EDS)[3] and cognitive impairment[4–6] related to repetitive hypoxia and sleep fragmentation.[4] EDS in OSA has been related to increased accident risk.[7]

A recent meta-analysis identified an elevated MVA risk ratio of 2.43 (95% confidence interval [CI] 1.21–4.89).[8] However, investigations of OSA and risk of MVA are hampered by a lack of objectively assessed MVA data and noncomparable methods or recruitment bias.[7,9–11] Uncertainty and recall bias may also reduce accuracy in terms of MVA classification. Furthermore, most studies failed to adjust for traffic exposure, defined as driving distance and time period,[12–14] which represent strong confounders in studies of MVA risk. A recent meta-analysis[15] including several studies[14,16–19] found that continuous positive airway pressure (CPAP) treatment reduced MVA risk by 72% (risk ratio of 0.28, 95% CI 0.22–0.35). However, limitations in terms of study design, power, incomplete CPAP compliance data, and/or reported MVA data reliability were identified. Only two smaller studies were based on objective MVA data.[14,17]

In order to overcome limitations in previous studies, we addressed a large, well-characterized patient cohort referred for OSA investigation. MVA incidence among these patients and a large control population from driver's license holders in the general population was obtained from the Swedish Traffic Accident Data Acquisition (STRADA) registry.[20] We hypothesized that accident rate is increased in patients with suspected OSA compared with the control population, that adequate treatment of the condition will reduce risk, and that specific clinical features in patients with OSA may be used to predict risk.

METHODS

The study was approved by the regional ethical review board in Gothenburg, Sweden. Patients provided written informed consent in association with an overnight diagnostic sleep study in the University Hospital.

Patient Population

An unselected sample of 1,718 consecutive clinical patients (age 18–80 y) referred for suspected OSA was included in the Gothenburg cohort of the multicenter European Sleep Apnea Database (ESADA)[21] study during the period 2007 to 2011 (flow chart 1). Participation in the ESADA study was on a voluntary basis and approximately 65.4% (n = 1,718) of all referred patients agreed to participate. Reported data included anthropometry, co-morbidity, smoking (yes/no) and alcohol habits (units/w), driver's license status (A/B, C/D/E, yes/no), driving distance (km/y), subjective sleepiness (Epworth Sleepiness Scale[22] [ESS]), habitual sleep time, and results from objective

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cardiorespiratory polygraphy recording (apnea-hypopnea index [AHI] and oxygen desaturation index [ODI]).[23] Data on license holding were missing in 46 cases and 194 patients were not license holders, leaving 1,478 license holders for the final analysis.

The STRADA Registry and the Control Population

The control population (n = 21,118) included individuals from the general population reported in the STRADA registry.[20] Individuals from the general population with a record of at least one MVA during the period 2002 to 2012 and with distribution of community of residency proportional to that of the patient population were included. The registry contains information on individual road traffic injuries and accidents from the entire Swedish national road transport system.[20] The information is reported by the Swedish police and the major emergency hospitals nationwide. The police at the site of the accident collected standardized information for registration in the STRADA. All types of accidents, including those involving pedestrians, bicycles, and trains/trams, are reported in the registry. The reported information includes geographical location, severity and cause of accident, type of accident, and degree of personal and property damage.

In this study, information on sex and age of the drivers holding a driver's license, and geographical location of the accident were acquired. All driver's license holders (n = 635,786) in the general population of the nine residential areas corresponding to the main hospital capture area were identified. Within this population we identified 21,118 drivers with an MVA record in the STRADA registry during the period 2002 to 2012. The estimation of the MVA risk was further stratified for existing regional driver's license (A/B or C/D/E) statistics provided by the Swedish transportation agency.[20]

Identification of Motor Vehicle Accidents among Patients

Driver's license holders (n = 1,478) in the clinical patient cohort were cross-analyzed with the STRADA registry. Police-reported MVAs in the time period between 2002 and 2012 were addressed. An observation period starting 5 y prior to the sleep diagnostic test and up to 5 y thereafter was evaluated. Investigators from the university hospital were blinded with respect to identity of patients in the STRADA database.

Assessment of OSA

All patients underwent a cardiorespiratory polygraphy recording (PG, Embletta X10 Portable Digital System, Embla CO, USA) during sleep according to clinical routine.[23] The recording included nasal pressure cannula, abdominal and thoracic respiratory effort belts, oximetry, body position, and recording time. Apneic and hypopneic events were scored when minimum event duration of 10 sec was found. Apnea-hypopnea index (AHI) was defined as the number of apneas/hypopneas during the recording session defined by lights off and lights on. Hypopnea, measured by the nasal cannula, was scored either when a $\geq$ 50% reduction of airflow followed by a $\geq$ 3% oxygen desaturation or a $\geq$ 30% reduction of airflow followed by a $\geq$ 4% oxygen desaturation was recorded.[24] AHI was explored both as a continuous and a categorical (mild/moderate/severe OSA according to AHI cutoffs of 5 $\leq$ 15, 15 $\leq$ 30 and $\geq$ 30 events/h, respectively) variable in the analysis. In the risk analysis, all patients undergoing a sleep diagnostic assessment, independent of outcome, were included in the analysis. Individuals with an AHI < 5 events/h were not considered as healthy controls.

CPAP and Compliance

CPAP prevents upper airway collapse[25] in OSA and was applied according to clinical routines (autoadjusting positive airway pressure (PAP), fixed-pressure PAP, or bilevel PAP in 85.5, 13.4, and 1.1% of cases, respectively). Information on CPAP usage time (h/night) was obtained from the device at follow-up visits and a CPAP use of $\geq$ 4 h/night was considered adequate compliance with therapy.[26] Individuals with limited CPAP use (< 4 h/night) or those who returned CPAP were classified as insufficiently compliant with therapy in the analysis. A mean follow-up time was calculated for each patient based on the event of diagnosis during the period 2007 to 2012.

In the current study, patients (n = 1,478) from the ESADA registry were cross-analyzed with police-reported information in the STRADA registry specifying a history of an MVA during a period of 5 y prior to and up to 5 y after the diagnostic sleep test. Information collected from the STRADA, included community of residency, sex, and age of the driver.

Statistics

MVA risk was calculated in R version 2.15.2 (© 2012, The R Foundation for Statistical Computing). All other statistics were calculated in PASW Statistics 17.0.2 (SPSS Inc. Chicago, IL, USA).

Data are presented as mean (standard deviation) and/or median [interquartile range], and a two-tailed $P < 0.05$ was considered statistically significant.

Analysis Comparing Motor Vehicle Accidents Risk in Patients Assessed for OSA and Control Population

Patients from the main hospital capture area, consisting of nine different residential regions, with a history of MVAs were stratified according to age (18–19, 20–24, 25–34, 35–44, 45–54, 55–64, 65–74, and $\geq$ 75–80 y) and calendar year (2002 to 2012) cohorts. The estimated risk analysis included 74 patients with a positive MVA history. Traffic accidents other than MVA were excluded (Figure 1).

In order to estimate the MVA rate in the control population, we assumed for each calendar year and age (cross-classified) stratum that (1) the driver's license status in the patient cohort did not change over time, and (2) that the number of driver's licenses (n = 635,786) in the different age categories were constant. For this assumption we used driver's license statistics from the calendar year 2012 and this was slightly nonconservative. However, sensitivity analyses of an increased number of driver's licenses from 2002 to 2012 did not differ from our estimated MVA risk. Realistic figures resulted in one or two additional accidents. Some of the accidents in the hospital capture area involved drivers residing outside the region, which in a conservative way makes risk estimates smaller. Conversely, approximately 10% of MVAs, caused by drivers living in the nine residential areas, occurred outside the study region. For each stratified year and age class the observed number of MVAs in

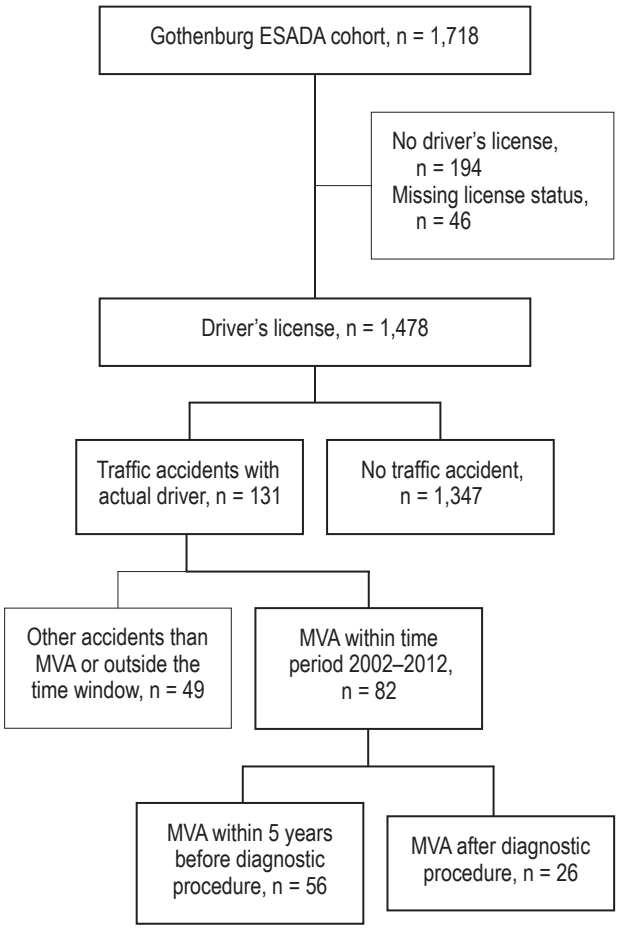

Figure 1—Study flow chart. ESADA, European Sleep Apnea Database; MVA, motor vehicle accident; STRADA, Swedish Traffic Accident Data Acquisition registry.

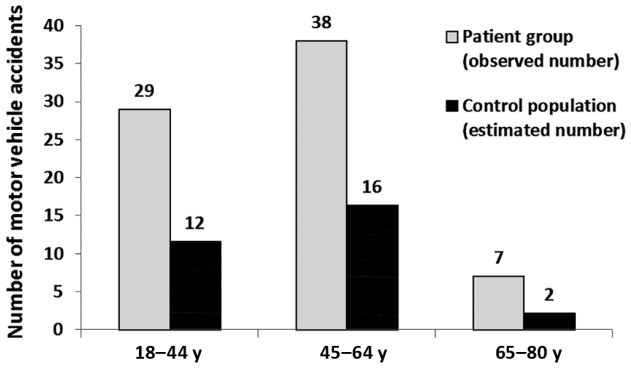

Figure 2—Observed number of accidents in the patient group compared with the expected number based on the control group, categorized into the corresponding age groups.

the patient cohort was multiplied with the estimated proportion of MVAs in the control population and the number of driver's license holders in that region. This was interpreted as an estimate of the expected number of MVAs in the patient cohort for that specific stratum given that there is no increased risk, and conditionally on the number of accidents in that stratum.

Finally, we summed all these expectations over the strata and used the actual number of MVAs in the patient cohort in all strata as a test variable. Under the null hypothesis assumption of no risk change, this test variable may be argued to be roughly Poisson distributed, conditional on all the total MVA figures in all the strata, with the sum of the aforementioned expectations, as its expectation. We used a one-sided test based on this Poisson approximation.

The null hypothesis was rejected if the number of observed MVAs in the patient cohort was found to be larger than the 95% quantile of a Poisson distribution, having the estimated expected number of MVAs in the control group as its parameter. Similarly, additional analyses were performed on MVAs in the patient cohort before and/or after sleep diagnostic test. Furthermore, we analyzed the observed numbers divided by the expected numbers under the null hypothesis, which may be interpreted as rough risk estimations of risk ratios. Figure 2 illustrates the estimated risk analysis. The observed number of accidents in the patient group was compared with the estimated number in the cross-classified control population. The accidents for patients and controls were categorized into three age groups accumulated and weighted by each stratum size (Figure 2).

Analysis of Risk Factors for Motor Vehicle Accidents in the Patient Cohort

The risk factor analysis included all clinical patients with suspected OSA with an MVA (n = 82) and without (n = 1,347) any type of traffic accident (TA), irrespective of residency and the geographic location of the accident. Nonparametric independent samples Mann-Whitney *U* test and Pearson chi-square were used for ordinal or quantitative data and for comparison of between group differences (Tables 1 and 2). Binary logistic regression was used for categorical response variable and independent categorical and continuous predictors (Table 3). Stepwise backward/forward likelihood ratio methods were used to test each predictor for the best model fit and adjusted for the year of diagnosis. Variables with a large continuous scale (e.g., driving distance) were standardized (z-score) in the analysis, but the unstandardized data were reported in order to facilitate meaningful interpretation. The time window for CPAP compliance was calculated from the number of follow-up days for each patient entering the study (2007 to 2012). The incidence of MVA/1,000 individuals/y was calculated before (2002 to 2007) and after CPAP.

RESULTS

Patient Population

The analysis included 1,478 patients (males 70.4%, mean age 53.6 (12.8) y, BMI 29.2 (5.5) kg/m^2, ESS score 10.6 (5.2) and median AHI 17.9 [3.2–24.2] events/h. Driver's license type A/B was reported by 84.2%, and 15.8% had a C/D/E license. A total of 82 MVAs were registered in the patient group and subsequently censored for this cohort (Figure 1). Of these, 56 MVAs occurred before diagnosis and 26 after diagnosis (Figure 1). Within the 5-y time period prior to the diagnostic sleep study, eight patients had two accidents and one patient had triple accidents. In the binary logistic regression analysis, only the most

Table 1—Characteristics of patients with motor vehicle accidents before and after diagnosis compared with patients with no traffic accidents.

	MVA BD (n = 56)	MVA AD (n = 26)	No TA (n = 1,347)	P All groups or BD vs. no TA, AD vs. no TA
Anthropometry				
Sex (male), %	75.9	76.9	69.7	≥ 0.3
Age, y	52.1 (14.5)	46.1 (14.5)	54.0 (12.7)	BD 0.5, AD 0.002
BMI, kg/m^2	30.0 (5.7)	30.0 (5.8)	29.0 (5.5)	≥ 0.2
OSA and Sleepiness				
AHI, n/h [a]	18.3 (20.5) 11.6 [3.2 to 24.3]	16.7 (19.9) 8.2 [3.6 to 20.9]	17.9 (20.9) 10.4 [3.2 to 24.7]	≥ 0.8
ODI, n/h [a]	16.9 (18.8) 10.5 [3.3 to 24.6]	14.5 (17.6) 6.8 [4.3 to 18.8]	17.0 (20.2) 10.4 [3.2 to 24.2]	≥ 0.7
Hab. sleep time, h [a]	7.4 (1.5)	7.3(1.8)	7.5 (1.3)	≥ 0.6
Hab. sleep time ≤ 5 h, %	7.1	15.4	4.2	BD 0.3, AD < 0.01
Hab. sleep latency, min [a]	32.6 (37.1) 30.0 [10.0 to 30.0]	37.8 (32.5) 30.0 [15.0 to 60.0]	31.9 (34.0) 20.0 [10.0 to 45.0]	≥ 0.2
ESS score	12.2 (5.5)	10.8 (5.1)	10.5 (5.1)	BD 0.02, AD 0.8
ESS ≥ 16	31.6	23.1	18.1	BD 0.01, AD 0.5
Comorbidity and Medication				
DM, %	17.2	11.5	10.1	≥ 0.08
CVD, %	39.7	42.3	46.2	≥ 0.3
Psychiatric disorder, % [a]	14.0	7.1	10.7	0.7
Hypnotic med. (ATC-N05), %	17.2	11.5	10.7	≥ 0.1
Psychoanaleptic med. (ATC-N06), %	19.3	3.8	17.1	≥ 0.07
Lifestyle Habits				
Alcohol consumption, units/w [a]	5.9 (10.4) 3.0 [0.0 to 7.2]	6.1 (6.2) 5.0 [1.0 to 9.0]	5.8 (7.9) 3.0 [0.0 to 8.0]	≥ 0.5
Smoking, %	19.6	19.2	14.9	≥ 0.3
Driving Habits				
Kilometers driven, 1,000/y [a]	26.0 (34) 15.0 [10 to 30]	26.0 (22) 20.0 [15 to 30]	18.0 (21) 15.0 [8 to 20]	BD 0.3, AD 0.001
C/D/E license, %	15.5	15.4	15.7	≥ 0.9

Statistics: Data are presented as mean (standard deviation) and/or median [range]. P ≤ 0.05 was considered significant. [a] Data completeness ≥ 83%. AD, after diagnostic sleep test; AHI, apnea-hypopnea index; ATC, anatomical therapeutic chemical classification; BD, before diagnostic sleep test; CVD, cardiovascular disease; DM, diabetes mellitus; ESS, Epworth Sleepiness Scale; Hab., habitual; MVA, motor vehicle accident; ODI, oxygen desaturation index; TA, traffic accident.

recent MVA was used. Patients with multiple accidents were younger than those with a single MVA (mean age 41.6 (11.6) and 51.3 (14.8), respectively, P = 0.06). No differences were found with regard to BMI (kg/m^2), AHI and ODI (events/h), ESS score, driving distance (km/y) or sex (all P ≥ 0.2).

Analysis Comparing Motor Vehicle Accidents Risk in Patients Assessed for OSA and Control Population

The estimated risk, calculated as the ratio between the observed and expected number of MVAs, both before and after diagnosis, as well as the total number of MVAs was between 2.3 to 2.6 times higher among patients compared with the control population (Table 4), adjusted for age, calendar year, and driver's license type. The observed estimated risk for MVA decreased gradually between the age groups 18–44, 45–64, and 65–80 y (Figure 2). But the strongest relative influence of OSA on MVA risk was found in the oldest age group (ratio 2.42, 2.37, and 3.50, respectively). The sex distribution was similar among patients with MVAs and the control population (male/female 75.6/24.4% and 70.6/29.4% respectively, P = 0.3).

The odds ratio for MVA-related injury in patients compared with the control population was 1.9 (95% CI 1.18–3.18, P < 0.01) after adjustment for age, year of accident, and sex.

The Motor Vehicle Accidents Risk Analysis in the Patient Cohort

Risk factors for MVA were evaluated among patients with a history of MVA and compared with patients without a history

Table 2—Baseline characteristics and motor vehicle accidents for patients with and without continuous positive airway pressure compliance.

	CPAP ≥ 4 h/night (n = 263)	CPAP < 4 h/night (n = 304)	P
Anthropometry			
Sex (male), %	77.9	72.4	0.1
Age, y	57.1 (10.5)	56.4 (11.6)	0.8
BMI, kg/m^2	30.6 (5.3)	29.5 (5.4)	0.02
Sleepiness and OSA			
Habitual sleep latency, minutes	23.3 (24.8) 15.0 [5.0 to 30.0]	32.1 (33.7) 25.0 [10.0 to 45.0]	0.002
Hab. sleep time, h	7.5 (1.2)	7.4 (1.4)	0.2
ESS score	11.6 (5.0)	10.7 (5.2)	0.02
AHI, n/h	30.2 (23.7) 23.4 [11.9 to 43.5]	22.3 (22.1) 14.9 [6.9 to 29.3]	< 0.001
CPAP usage, h/night	5.8 (1.3)	1.4 (1.5)	< 0.001
Comorbidity and Medication			
DM, %	16.3	13.5	0.3
CVD, %	60.1	55.6	0.3
Psychiatric disorder, %	9.8	11.2	0.6
Insomnia, %	0.4	2.0	0.09
Hypnotic med. (ATC-N05), %	7.6	10.5	0.2
Psychoanaleptic med. (ATC-N06), %	17.9	13.5	0.1
Lifestyle			
Smoking, %	12.5	16.4	0.2
Alcohol consumption ≥ 10 units/w	5.8 (6.7) 5.0 [1.0 to 8.0]	6.2 (7.1) 4.0 [0.0 to 9.7]	0.9
Driving Habits			
DL (CDE), %	19.4	18.1	0.7
MVA, n (%)	3.0 (1.2)	13.0 (4.4)	< 0.02
Kilometers driven, 1,000/y	20.0 (20) 15.0 [10 to 25]	18.0 (22) 15.0 [5 to 20]	0.002

Statistics: chi-square, data are presented as mean (standard deviation) and/or median [range], P ≤ 0.05 was considered significant. AHI, apnea-hypopnea index; ATC, anatomical therapeutic chemical classification; CPAP, continuous positive airway pressure; CVD, cardiovascular disease; DL, driver's license; DM, diabetes mellitus; ESS, Epworth Sleepiness Scale; Hab., habitual; km, kilometers; MVA, motor vehicle accident.

Table 3—Independent predictors associated with motor vehicle accidents among patients with obstructive sleep apnea – results from the multivariable regression analysis.

	Estimate (SE)	OR	95% CI for OR	P
Age, y	−0.019 (0.010)	0.98	0.962 to 1.000	0.05
Hab. sleep time ≤ 5 h	0.96 (0.43)	2.66	1.14 to 6.01	0.02
ESS score ≥ 16	0.76 (0.27)	2.13	1.26 to 3.61	0.005
Hypnotic use	0.73 (0.33)	2.07	1.07 to 3.98	0.03
Driving distance, 10,000 km/y	0.085 (0.04)	1.09	1.01 to 1.18	0.03
Sex (male)	0.33 (0.30)	1.42	0.78 to 2.45	0.2
DL type, (C/D/E)	−0.04 (0.35)	0.92	0.536 to 2.02	0.9
Diagnosis y	−0.13 (0.09)	0.88	0.74 to 1.05	0.9
Constant	251.0 (179.0)			0.2

R^2 = 0.05 (Hosmer and Lemeshow), 0.07 (Nagelkerke). Model chi-square = 30.7, P < 0.001. P < 0.05 was considered significant. CI, confidence interval; DL, driver's license; ESS, Epworth Sleepiness Scale; Hab., habitual; OR, odds ratio; SE, standard error.

Table 4—The expected number of motor vehicle accidents used as a parameter of a Poisson distribution.

	Expected MVA, n	95% Quantile	Observed MVA, n	Observed/Expected	P
Before diagnosis	19.14	27	49	2.56	$2.48\ E^{-09}$
After diagnosis	11.04	17	25	2.26	$7.35\ E^{-05}$
Total	30.19	39	74	2.45	$3.30\ E^{-12}$

The number of observed motor vehicle accidents in the patient cohort was compared with the 95% quantile of the respective Poisson distribution. MVA, motor vehicle accident.

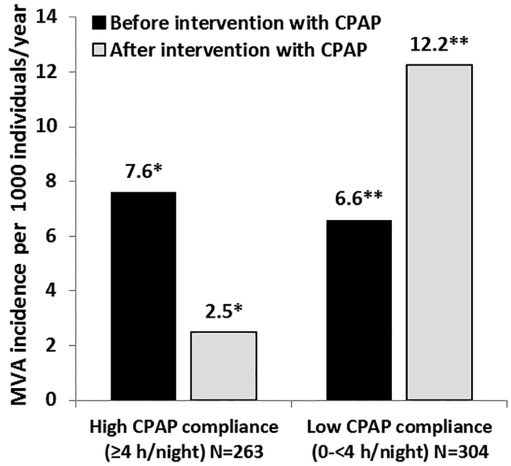

Figure 3—Incidence of motor vehicle accidents (MVAs) per 1,000 individuals per year before and after continuous positive airway pressure (CPAP) intervention. Statistics: * 70% reduction, ** 54% increase.

of any type of traffic accident (Table 1). Patients with an MVA before diagnosis had a higher ESS score, whereas those with an MVA after diagnosis were younger, more frequently reported a short subjective sleep time (≤ 5 h/night), less frequently psychoanaleptic drug users, and had longer driving distances (Table 1). Sex, BMI, and prevalence of comorbidities did not differ between groups (Table 1). Variables describing severity of the OSA condition (AHI, ODI) were similar in all groups (all $P \geq 0.3$).

In the logistic regression analysis, short sleep duration, severe EDS (ESS ≥ 16), and use of hypnotic drugs all independently provided more than 2.0-fold increased odds for an MVA (Table 3). Young age and elevated driving distance were associated with 2% and 9% higher odds for an MVA, respectively (Table 3). No associations were found between MVA and sex or driver's license type (Table 3).

Patients (n = 567) with available CPAP treatment data had a mean follow-up time of 3.5 (1.0) y. However, 38% of the patients returned their CPAP (CPAP off), 15.5% used CPAP with low compliance (< 4 h/night), and 46.5% were highly compliant CPAP users (≥ 4 h/night). Median CPAP compliance was 0.0 (0.0 to 2.0), 2.0 (1.0 to 3.0), and 6.0 (5.0 to 7.0) h/night, respectively. The number of MVAs among patients in whom OSA had been diagnosed without information on treatment (n = 462) was reduced by 62% (9.5–4.0 incidence of MVA/1,000 individuals/y) following diagnosis.

The MVA incidence was reduced by 70.0% among patients with high CPAP (≥ 4 h/night) compliance, whereas it increased by 54.0% among noncompliant patients (< 4 h/night or off CPAP) (Figure 3). During the corresponding time window from 2007 to 2012, there was an observed decrease of accidents by 15.9% in the STRADA. Patients with high compliance had fewer MVAs, a higher AHI, BMI, ESS score, and annual driving distance at the time of diagnosis compared with the low compliance group (Table 2). No group differences were found at baseline with respect to sex, age, comorbidity, and smoking and alcohol consumption (Table 2).

DISCUSSION

This large-scale retrospective cohort study using national traffic accident statistics provides strong evidence for a link between sleep apnea and traffic safety. Patients with OSA had more frequent MVAs, and injury following the accidents was more common when compared with the control population. Effectively used CPAP therapy was associated with a reduction of MVA frequency. Severe daytime sleepiness, but not severity of sleep apnea, was identified as a risk factor for MVA in patients with OSA.

The current study found a 2.5-fold increased MVA risk in patients with OSA, which is in line with previous findings.[8] Our data extend current knowledge in several aspects. First, our MVA reports are based on high-quality, objectively reported accident information by police officers at the scene. Questionnaire-based reports on MVAs are generally considered as of limited confidence.[8,14] Moreover, current data on objective MVA reports may be limited because of the inconsistent source of information (police/insurance company/driver) and the variable format of accident reports.[2,16] For example, Findley et al.[14] used a governmental registry containing data provided by the driver involved in the accident and/or the state police. Second, we only included accidents where the subject was the actual driver involved in the MVA. Third, our study is the largest so far to be based on objective MVA data and classification of personal injury related to the accident. Finally, national accident statistics suggest that the influence of OSA on traffic safety may be particularly well studied in the realm of the current statistics. Sweden is, in terms of traffic safety standards, considered as a leading country and the reported MVA-related death rate is the lowest in Europe ($28/10^6$ inhabitants compared to European mean of $68/10^6$ during 2010).[27] It may therefore be speculated that the effect of OSA on MVA frequency and injury rate may be even higher in other areas of Europe or the world.

The predictors of increased MVA risk in patients with OSA remain unclear and generate a challenge in clinical medicine. OSA severity (e.g., AHI or ODI) appear to only poorly predict

actual crash risk, and our findings were in line with previous reports suggesting that risk of accident is complex to predict on an individual basis in patients with sleep apnea. Subjectively assessed EDS has been shown to be associated with self-reports of near-miss crash rates.[28] Objective assessment of daytime sleepiness by the Multiple Sleep Latency Test (MSLT) or the Maintenance of Wakefulness Test (MWT)[4] have been proposed as reliable predictors of MVA risk among patients with hypersomnia.[29] However, these methods produced conflicting data in a study of patients with sleep disordered breathing.[12] However, we identified several additional factors previously shown to associate with MVA risk, such as severe subjective daytime sleepiness (ESS score ≥ 16), long annual driving distance,[30] use of hypnotic medication,[31] young age,[1,32] and short self-reported sleep time.[30] Not only would there be a high degree of interaction between these risk factors, it is also likely that they are not sufficiently specific for the condition of sleep apnea alone. For instance, frequent driving is linked to shortened sleep time,[30] younger individuals are known to experience daytime sleepiness irrespective of sleep apnea,[3] shortened sleep time is associated with increased degree of sleepiness,[33] and hypnotic medication use may induce compromised alertness and performance deficits in driving tests.[31] Other potential confounders accounted for in our study, but not shown to influence MVA risk, included diabetes, alcohol, body composition measures, psychotropic medication, insomnia diagnosis, and sex. Future medicolegal regulations on driving in sleep apnea therefore need to jointly address the interaction between the condition and its treatment, the driver, and the circumstances of driving in a more general perspective.

CPAP is highly effective in eliminating sleep apnea thereby improving sleep quality and overnight oxygenation. Consequently, therapy is expected to result in improved daytime alertness and better driving performance. In addition, awareness of an OSA diagnosis and interaction with a professional health care environment is highly likely to increase awareness of the risk of sleepy driving.

Findley et al.[14] assessed the number of automobile accidents before and after successful treatment with nasal CPAP. Crash rate was eliminated after CPAP but remained unchanged in patients with untreated OSA.[14] However, this was a small study and CPAP compliance was determined by a telephone interview. Another study conducted by George et al.[17] found a threefold higher MVA ratio (0.18 versus 0.06 crashes/driver/y) based on collision reports in untreated patients. This risk was normalized following CPAP.[17] However, information on the type of accident and objective CPAP compliance was not provided. Other studies of the CPAP effect consistently lack objective assessment of MVA frequency.[16,34]

In a recent meta-analysis conducted by Tregear et al.,[15] nine retrospective studies evaluating the effect of CPAP on MVA risk were examined.[11,14,16–19,34–36] Only two of the nine studies were controlled and based on objective MVA data.[14,17] The overall MVA risk reduction in patients with severe OSA was 65–78% following CPAP (risk ratio 0.278, mean 0.22–0.35, $P < 0.01$).[15] In addition, our data show, for the first time, that MVA risk reduction is confined to patients who comply with therapy for at least 4 h/night. This threshold effect of CPAP therapy has been reported for blood pressure treatment in patients with hypertension[37] as well as in a study addressing subjective and objective measures of daytime alertness.[26] Somewhat unexpectedly we found that patients with lower CPAP compliance paradoxically had an increased MVA frequency, suggesting that incomplete CPAP use is linked to high traffic accident risk. The most likely explanation for this finding is that noncompliant patients, in terms of lifestyle, constitute a group that is less health focused and more risk prone. This finding, however, would remain as speculation because we were unable to identify markers of an unhealthy lifestyle, including nicotine/alcohol consumption, obesity, and/or specific comorbidities, in the noncompliant group. In fact, driving exposure was even lower among these patients. Interestingly, sleep latency was significantly increased in the noncompliant CPAP group, a finding that potentially may reflect an influence of comorbid insomnia.[38]

Our study adds to the field because it controlled for several factors of importance for the association between sleep apnea and traffic accidents including objective and standardized MVA characterization, stratification of residency and driver's license type, traffic exposure, nationwide coverage of MVA reports, phenotyping of OSA severity and risk factors for sleepy driving, assessment of treatment compliance by means of objective CPAP-log data, and a large sample size.

Despite these strengths, some study limitations need to be mentioned. The current study addresses a clinical sleep apnea cohort. It cannot be excluded that patients with OSA seeking medical attention to a higher extent may represent individuals who previously have experienced sleepiness behind the wheel, a near-miss accident, or even an actual MVA. Data therefore may not be generally extrapolated to the general effect of sleep apnea on traffic safety. However, the MVA frequency was evenly distributed throughout the years and did not accumulate directly prior to the referral for sleep testing. We lacked detailed information on type and effectiveness of treatment in a subgroup of 462 patients. It is assumed that most of these patients received therapy in line with conventional routines. Nevertheless, we found a reduced incidence of MVAs in this group suggesting that, in addition to the overall background reduction of MVAs during the period 2002–2012, there appeared to be an effect of intervention that unfortunately escaped detection because of incompleteness of data. Furthermore, data on actual annual driving distance and degree of daytime sleepiness in the general population subsample is incomplete. To control for traffic density and exposure to traffic, the patient cohort as well as the control population were stratified for age, geographic region based on the hospital capture area, and information on driver's license type. It is noted that the accident rate in this study, approximately 0.002, is substantially lower than that reported in previous studies (0.02, 0.07, 0.08).[2,14,34] Possible explanations include statistics showing a substantial reduction of MVA during the past decade, the high national traffic safety standards, and most importantly the proportionally stricter criteria for an MVA definition applied. Finally, excessive sleepiness was defined by means of the ESS. Because the ESS is a subjective measure, it is prone to recall bias and a systematic underestimation particularly among commercial drivers. Therefore, these factors are likely to increase variance in the statistical models used to predict MVA risk in OSA. The

exploratory risk factor analysis suggests the need for further data collection, in particular concerning the role of CPAP compliance.

CONCLUSION

Our study provides strong evidence that untreated OSA increases the risk of MVA and this is influenced by severe daytime sleepiness. Apnea events do not predict MVA risk but OSA treatment with CPAP leads to considerable risk reduction. Identification of MVA risk prone individuals remains to be a challenge in the management of patients with OSA. Importantly, patients using CPAP who are not in compliance may require specific attention in the clinical assessment of MVA risk.

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SUPPLEMENTAL MATERIAL

Table S1—Characteristics of the general control population obtained from the Swedish traffic accident data acquisition registry (STRADA) stratified by age and calendar year.

	Age Class	N	Age (y) mean (SD)	Sex, (male, %)
All	18–19	878	18.6 (0.5)	73.1
	20–24	2,703	21.9 (1.4)	73.7
	25–34	4,722	29.6 (2.9)	69.4
	35–44	4,936	39.5 (2.9)	67.8
	45–54	3,841	49.2 (2.9)	71.5
	55–64	2,641	59.1 (2.8)	72.4
	65–74	1,021	68.8 (2.9)	71.2
	75–80	376	77.3 (1.7)	72.1
Total	18–80	21,118	40.5 (14.8)	70.6
2002	18–19	76	18.7 (0.5)	84.2
	20–24	277	21.8 (1.4)	76.2
	25–34	514	29.5 (2.9)	73.7
	35–44	537	39.2 (2.9)	69.8
	45–54	344	49.2 (3.0)	71.8
	55–64	267	58.7 (2.8)	72.7
	65–74	87	68.9 (2.9)	69.0
	75–80	42	77.4 (1.8)	81.0
2003	18–19	84	18.6 (0.5)	75.0
	20–24	304	21.9 (1.4)	78.9
	25–34	509	29.8 (2.9)	68.4
	35–44	519	39.3 (2.8)	70.1
	45–54	376	49.4 (3.0)	71.8
	55–64	284	59.1 (2.8)	75.4
	65–74	92	68.9 (2.8)	72.8
	75–80	42	77.3 (1.8)	85.7
2004	18–19	104	18.6 (0.5)	72.1
	20–24	302	21.8 (1.4)	73.8
	25–34	480	29.4 (2.8)	72.3
	35–44	504	39.5 (2.9)	67.1
	45–54	353	49.0 (2.9)	72.8
	55–64	244	59.1 (2.7)	77.9
	65–74	85	68.6 (2.8)	82.4
	75–80	35	77.4 (1.7)	62.9
2005	18–19	83	18.5 (0.5)	69.9
	20–24	270	22.3 (1.4)	73.0
	25–34	504	29.6 (2.8)	71.2
	35–44	520	39.2 (2.8)	67.7
	45–54	354	49.2 (2.9)	70.3
	55–64	259	59.0 (2.9)	70.7
	65–74	80	69.2 (3.0)	76.3
	75–80	34	77.9 (1.6)	61.8
2006	18–19	99	18.6 (0.5)	73.7
	20–24	315	22.0 (1.4)	74.6
	25–34	525	29.5 (3.0)	64.0
	35–44	503	39.6 (2.9)	68.4
	45–54	377	49.4 (2.8)	73.2
	55–64	251	59.0 (2.8)	69.7
	65–74	103	69.2 (3.1)	74.8
	75–80	44	76.7 (1.6)	70.5
2007	18–19	94	18.6 (0.5)	70.2
	20–24	275	22.0 (1.4)	73.8
	25–34	466	29.5 (2.8)	71.9
	35–44	486	39.6 (2.9)	71.2
	45–54	367	49.1 (2.8)	70.6
	55–64	270	59.1 (2.7)	71.5
	65–74	99	68.9 (2.9)	69.7
	75–80	43	77.2 (1.8)	67.4
2008	18–19	80	18.5 (0.5)	76.3
	20–24	208	21.9 (1.4)	71.6
	25–34	389	29.6 (2.9)	69.4
	35–44	417	39.7 (2.9)	63.8
	45–54	353	49.1 (2.9)	70.8
	55–64	220	59.0 (2.9)	71.8
	65–74	100	68.5 (3.1)	71.0
	75–80	34	77.2 (1.7)	82.4
2009	18–19	65	18.6 (0.5)	73.8
	20–24	173	22.1 (1.4)	72.3
	25–34	323	29.7 (2.9)	67.8
	35–44	343	39.6 (2.8)	65.9
	45–54	304	49.5 (2.9)	70.1
	55–64	175	59.2 (2.8)	75.4
	65–74	78	68.6 (2.8)	71.8
	75–80	25	77.5 (1.8)	68.0
2010	18–19	64	18.6 (0.5)	70.3
	20–24	197	21.9 (1.4)	68.5
	25–34	348	29.3 (2.9)	67.8
	35–44	394	39.7 (2.9)	66.5
	45–54	358	49.1 (2.8)	68.7
	55–64	225	59.2 (2.9)	71.1
	65–74	99	68.7 (2.8)	68.7
	75–80	30	77.2 (1.7)	76.7
2011	18–19	70	18.6 (0.5)	65.7
	20–24	198	22.0 (1.4)	70.2
	25–34	347	29.6 (2.9)	67.4
	35–44	390	39.4 (2.9)	67.9
	45–54	334	49.2 (2.9)	76.3
	55–64	239	59.2 (2.9)	68.2
	65–74	99	68.7 (2.9)	68.7
	75–80	25	77.4 (1.6)	64.0
2012	18–19	58	18.6 (0.5)	74.1
	20–24	183	21.8 (1.5)	72.7
	25–34	317	29.6 (2.9)	67.2
	35–44	323	39.6 (2.8)	64.7
	45–54	321	49.2 (2.8)	70.1
	55–64	206	59.1 (3.0)	72.3
	65–74	98	68.5 (2.7)	60.2
	75–80	22	77.6 (1.8)	63.6

SD, standard deviation.