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BRIEF COMMUNICATION

Ten-Year Trends in Sleep-Disordered Breathing After Ischemic Stroke: 2010 to 2019 Data From the BASIC Project

Sonja G. Schütz, MD, MS, MSc; Lynda D. Lisabeth, PhD; River Gibbs, MS; Xu Shi, PhD; Ronald D. Chervin, MD, MS; Madeline Kwicklis, MS; Erin Case, BA; Devin L. Brown, MD, MS

BACKGROUND: Despite good evidence that the prevalence of sleep-disordered breathing (SDB) is increasing in the general population, no data are available about trends in poststroke SDB. We therefore sought to assess changes in poststroke SDB over a 10-year period (2010–2019).

METHODS AND RESULTS: Participants in the BASIC (Brain Attack Surveillance in Corpus Christi) project were offered a home sleep apnea test to assess for SDB after stroke. SDB assessment procedures remained unchanged throughout the study period. Respiratory event index was calculated as the sum of apneas and hypopneas per hour of recording. SDB was defined as respiratory event index ≥10/h for optimal sensitivity and specificity of the home sleep apnea test device compared with in-laboratory polysomnography. Regression models were used to test associations between SDB prevalence and severity and time, with adjustment for multiple potential confounders. Among the 1215 participants who completed objective sleep apnea testing, the prevalence of SDB grew from 61% in the first year of the study to 76% in the last, with 1.1 times higher odds each year (95% CI, 1.07–1.19), after adjustment. A linear association was identified between time and respiratory event index (average annual respiratory event index increase of 0.56/h; 95% CI, 0.20/h–0.91/h), after adjustment. There was no difference in time trends by sex or ethnicity.

CONCLUSIONS: The prevalence and severity of SDB after ischemic stroke has increased over the past 10 years in this population-based cohort. These data highlight the need to determine whether SDB treatment improves stroke outcomes.

Key Words: cerebrovascular disease ■ ischemic stroke ■ obstructive sleep apnea ■ sleep-disordered breathing

Sleep-disordered breathing (SDB) and stroke are both highly prevalent disorders.[1,2] According to a recent meta-analysis, the prevalence of SDB exceeds 70% in adults after stroke in cross-sectional studies.[3] SDB is a risk factor for both incident and recurrent stroke, and is associated with poor functional and cognitive outcomes after stroke.[4]

In the general population, the prevalence of SDB has increased in recent years.[5] However, time trends in SDB after stroke have not been characterized. This population-based surveillance study in individuals with recent ischemic stroke sought to assess changes in prestroke SDB risk and poststroke SDB prevalence and severity over a 10-year period.

METHODS

The study data are not available to other investigators as this process is not covered by the informed consent document. This study was approved by the Institutional Review Boards of the University of Michigan and Corpus Christi hospital systems. Written informed consent was obtained from all participants or a surrogate.

Correspondence to: Devin L. Brown, MD, MS, University of Michigan, 1500 E Medical Center Dr, Ann Arbor, MI 48109. E-mail: devinb@umich.edu

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Study Participants and Procedures

The BASIC (Brain Attack Surveillance in Corpus Christi) project is a population-based stroke surveillance study conducted in all acute care hospitals in Nueces County, Texas. This study uses active and passive surveillance to identify all cases of stroke among adults aged ≥45 years who are Nueces County residents. BASIC study methods have been published previously in detail.[6] All stroke cases are validated by stroke-trained physicians. A baseline interview, including the Berlin Questionnaire[7] to assess SDB risk in reference to the prestroke state, is conducted as soon as possible after ischemic stroke presentation. Demographic information, National Institutes of Health Stroke Scale, and medical comorbidities are abstracted from the medical record. Excessive alcohol use is coded as present if excessive alcohol consumption is documented in the medical record.

Sleep Apnea Testing and Definitions

All participants in BASIC were offered a home sleep apnea test (ApneaLink Plus; ResMed, San Diego, CA) within 30 days of ischemic stroke if identified by active surveillance (screening of admission logs and canvassing inpatient units for stroke cases) or 45 days if identified by passive surveillance (based on discharge diagnosis codes),[6] if they were not excluded based on use of supplemental oxygen, current mechanical or positive pressure ventilation, or pregnancy. The ApneaLink Plus monitors nasal pressure (airflow), oxygen saturation, pulse, and respiratory effort. Apneas were defined as nasal pressure decrease of ≥80% for ≥10 seconds. Using ApneaLink's default criteria and settings, hypopneas were defined as airflow signal decrease of ≥30% but <80% for ≥10 seconds, associated with a decrease in oxygen saturation of ≥4% (unless oximetry was missing for a significant portion of the recording, in which case hypopneas were defined as a reduction of nasal pressure of ≥30% for ≥10 seconds per ApneaLink's algorithm). The correlation in apnea-hypopnea index between automatically scored ApneaLink Plus and manually scored full in-laboratory polysomnography is 0.97.[8] The same registered polysomnographic technologist reviewed the initial automated scoring throughout the study,[9] adjusted any inappropriately scored events, edited start and stop times, eliminated artifacts, removed incorrectly scored events, and added missed events consistent with ApneaLink's scoring criteria. ApneaLink studies with interpretable evaluation periods <2 hours were excluded. The respiratory event index (REI) was calculated as the sum of apneas and hypopneas per hour of recording. SDB was defined as REI ≥10/h. SDB assessment procedures remained unchanged from 2010 to 2019.

Statistical Analysis

Logistic (SDB and prestroke SDB risk) and linear (REI) regression models were used to test associations with time (parameterized as years since 2010), with and without adjustment for prespecified potential confounders. Age (centered at median), sex, race and ethnicity, body mass index (centered at median), hypertension, diabetes, tobacco use, history of prior stroke/transient ischemic attack, excessive alcohol use, coronary artery disease, hypercholesterinemia, and National Institutes of Health Stroke Scale scores were included in the multivariable logistic regression model for prestroke SDB risk. Regression models of poststroke SDB and REI were adjusted for the above variables and history of congestive heart failure and prestroke sleep apnea risk (ie, dichotomous Berlin Questionnaire score). In separate models, an interaction term for time×ethnicity or time×sex was added. All analyses were conducted using SAS 9.4 (SAS Institute Inc, Cary, NC). The authors had full access to all the data and take responsibility for their integrity and data analysis.

Table 1. Baseline Characteristics

Characteristic	Berlin Questionnaire completed (n=2811)	ApneaLink study completed (n=1215)
Age, median (IQR), y	68.0 (59.0–79.0)	65.0 (57.0–74.0)
Men, n (%)	1429 (51)	648 (53)
Mexican American, n (%)	1748 (62)	794 (65)
Hypertension, n (%)	2346 (84)	1018 (84)
Diabetes, n (%)	1378 (51)	656 (54)
Atrial fibrillation, n (%)	418 (15)	124 (10)
Current tobacco use, n (%)	1150 (41)	521 (43)
Prior stroke/transient ischemic attack, n (%)	808 (29)	342 (28)
Excessive alcohol, n (%)	177 (6)	81 (7)
Congestive heart failure, n (%)	305 (11)	99 (8)
Coronary artery disease, n (%)	829 (30)	351 (29)
Dyslipidemia, n (%)	1412 (51)	629 (52)
NIH Stroke Scale score, median (IQR)	4.0 (1.0–8.0)	3.0 (1.0–6.0)
Body mass index, median (IQR), kg/m^2	28.2 (24.8–32.8)	29.0 (25.5–33.4)
Prestroke high risk of sleep apnea (Berlin Questionnaire), n (%)	1723 (61)	765 (63)
Sleep-disordered breathing (REI ≥10/h), n (%)	…	831 (68)
REI, median (IQR)	…	16 (8–28)
Central apnea index, median (IQR)	…	0 (0–2)

IQR indicates interquartile range; NIH, National Institutes of Health; and REI, respiratory event index.

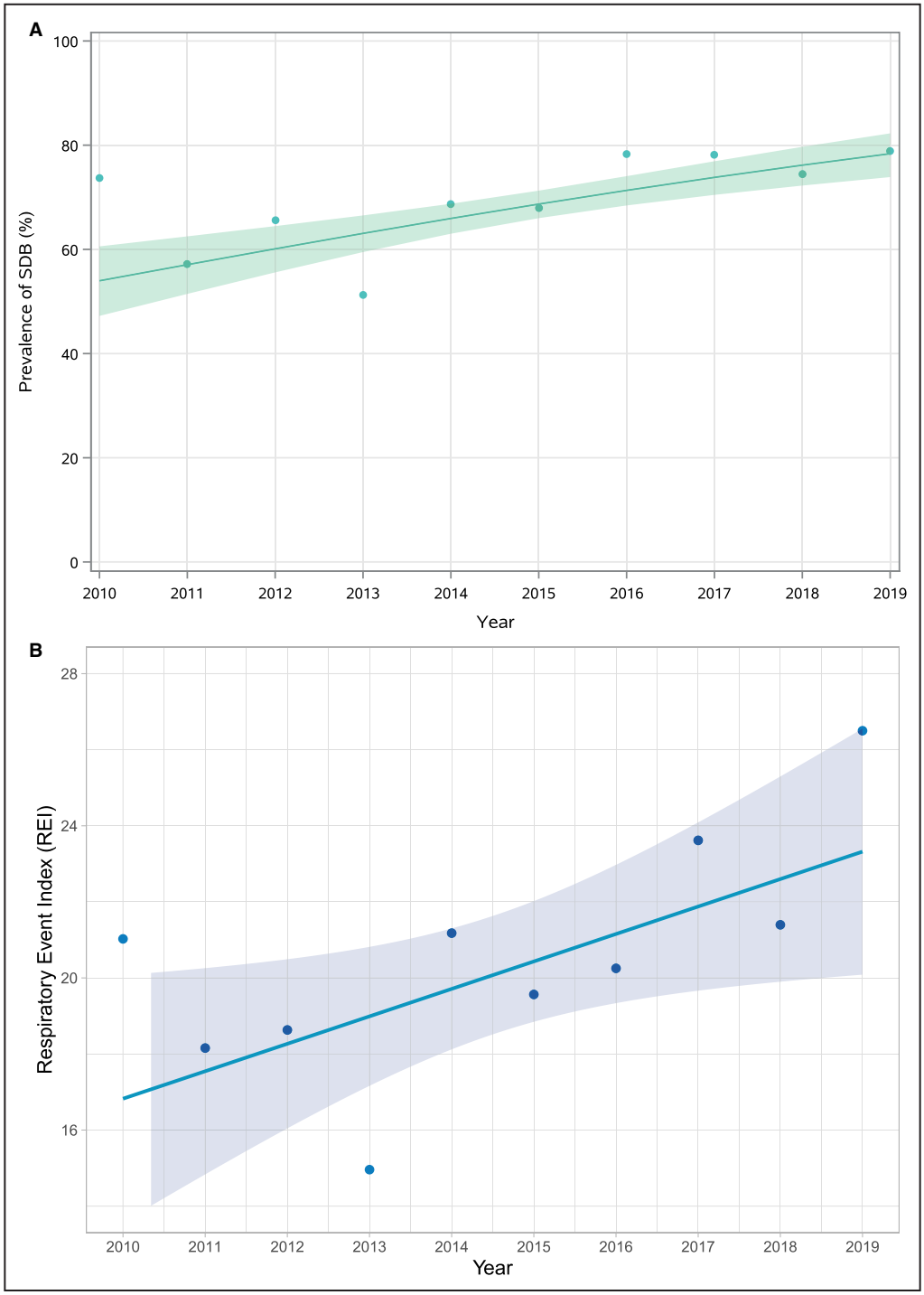

Figure. Time trends in sleep-disordered breathing (SDB) prevalence and severity, 2010 to 2019. **A**, SDB prevalence (points), 2010 to 2019, with regression line and 95% CI (shaded region) based on unadjusted logistic regression. **B**, Median respiratory event index (REI) (points), 2010 to 2019, with regression line and 95% CI (shaded region) based on unadjusted linear regression.

RESULTS

A total of 2811 participants completed the Berlin Questionnaire in reference to the prestroke state shortly after presenting with new-onset ischemic stroke (median, 8 days; interquartile range, 3–40 days). Among the subgroup of 1489 who consented to ApneaLink Plus testing, 1215 participants had ApneaLink Plus data available (median, 12 days after stroke; interquartile range, 6–21 days after stroke), and these subjects had baseline

Table 2. Multivariable Models of Associations Between Time and SDB or REI

Variable	Association between time and categorical SDB (REI >10/h), adjusted odds ratio (95% CI)	Association between time and continuous REI, adjusted β (95% CI)
Intercept	0.35 (0.22 to 0.58)	6.77 (3.52 to 10.01)
Time, y	1.13 (1.07 to 1.19)	0.56 (0.20 to 0.91)
Men/women	2.47 (1.86 to 3.26)	6.77 (4.97 to 8.56)
Mexican American/non-Hispanic White ethnicity	1.60 (1.21 to 2.11)	2.02 (0.17 to 3.87)
Age	1.02 (1.01 to 1.03)	0.17 (0.09 to 0.26)
Hypertension	1.58 (1.09 to 2.28)	3.29 (0.74 to 5.85)
Diabetes	1.07 (0.80 to 1.42)	1.53 (–0.34 to 3.39)
Current tobacco use	0.69 (0.52 to 0.91)	–1.79 (–3.60 to 0.02)
Prior stroke/transient ischemic attack	1.27 (0.93 to 1.73)	1.78 (–0.16 to 3.73)
Excessive alcohol	1.06 (0.62 to 1.81)	–1.04 (–4.54 to 2.47)
Congestive heart failure	1.00 (0.60 to 1.67)	0.57 (–2.68 to 3.82)
Coronary artery disease	1.00 (0.73 to 1.38)	1.70 (–0.33 to 3.73)
High cholesterol	0.97 (0.73 to 1.29)	0.05 (–1.77 to 1.87)
NIH Stroke Scale score	1.00 (0.98 to 1.03)	0.12 (–0.04 to 0.29)
Body mass index	1.07 (1.04 to 1.10)	0.46 (0.31 to 0.60)
Prestroke high risk of sleep apnea (Berlin Questionnaire)	1.20 (0.90 to 1.59)	0.82 (–1.07 to 2.71)

NIH indicates National Institutes of Health; REI, respiratory event index; and SDB, sleep-disordered breathing.

characteristics comparable to the larger sample of 2811 participants with Berlin Questionnaire data (Table 1).

The prevalence of SDB after ischemic stroke increased from 61% to 76%, and mean REI increased from 18.7±15.7/h to 22.9±18.1/h between 2010 and 2019 (Figure [A and B]). A linear association was identified between time and presence of SDB in the unadjusted analysis (1.13 times higher odds/year; 95% CI, 1.08–1.19 times higher odds/year) and after adjustment (1.13 times higher odds/year; 95% CI, 1.07–1.19 times higher odds/year) (Table 2). Time trends did not differ by sex (P=0.24) or ethnicity (P=0.36). Similarly, there was a linear relationship between time and continuous REI in the unadjusted analysis (mean annual increase, 0.66/h; 95% CI, 0.30/y–1.03/y) and after adjustment (mean annual increase, 0.56/h; 95% CI, 0.20/h–0.91/h). Time trends in REI did not differ by sex (P=0.91) or ethnicity (P=0.97). Also, a trend toward a linear association between time and high prestroke risk of SDB was found in the unadjusted analysis (1.03 times higher odds/year; 95% CI, 1.00–1.06 times higher odds/year; P=0.08), although not in the adjusted analyses (1.02 times higher odds/year; 95% CI, 0.99–1.05 times higher odds/year; P=0.21) (Table S1).

DISCUSSION

In this large population-based cohort of participants with recent ischemic stroke, the prevalence of SDB after ischemic stroke increased by 15% over the 10-year study period, whereas mean REI increased from 19/h to 23/h. The increase in poststroke SDB prevalence and severity over time remained significant after adjustment for multiple potential confounders, including body mass index. Time trends were similar by sex and ethnicity. Despite a trend before adjustment for potential confounders, prestroke SDB risk did not significantly increase over the decade studied.

These novel findings confirm a high prevalence of SDB after stroke,[3] with 3 of 4 individuals affected in recent years in our cohort. Awareness of the high and increasing prevalence of SDB after stroke is important for providers given that SDB treatment might improve stroke outcomes.[10] As expected, central sleep apnea was uncommon among these poststroke participants.[11]

The reasons for the increasing prevalence of SDB after stroke remain unclear. A change in study procedures or SDB scoring criteria does not account for our findings given our stable study procedures and scoring algorithm. Our results mirror the increasing prevalence of sleep apnea in the general population[5]; however, the data also suggest that increasing prestroke SDB does not fully explain increasing poststroke SDB, given that the relationship persisted despite adjustment for prestroke SDB risk. It is possible that the increase in poststroke SDB is attributable to unmeasured SDB risk factors that changed commensurately (eg, environmental factors, increasingly sedentary lifestyle, increasing sleep deprivation which may exacerbate obstructive sleep apnea, or redistribution of weight within constant body mass index strata).

The strengths of this study include a large and diverse population-based sample, validation of ischemic

stroke by trained stroke physicians, systematic data collection, and application of a well-validated sleep apnea test. A limitation is the lack of validation of the Berlin Questionnaire to assess stroke patients' risk of SDB in reference to the prestroke state, although it is well validated in the general population[12] and has been used similarly before.[13] As this study recruited participants from a single county in Texas, which includes a high proportion of Mexican Americans, the results may not be generalizable to the general US or other populations. Similarly, because this study population included mostly participants with low National Institutes of Health Stroke Scale scores, it is possible that the findings may not be generalizable to patients whose strokes led to severe neurologic deficits. The automated scoring of the ApneaLink Plus studies was reviewed and edited where necessary by a registered polysomnographic technologist, aiming to quantify the degree of SDB based on standardized scoring criteria, but not to arrive at a clinical diagnosis of obstructive sleep apnea, which would warrant physician review and interpretation of the test.

ARTICLE INFORMATION

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Affiliations

Department of Neurology (S.G.S., R.D.C., D.L.B.), Department of Epidemiology (L.D.L., R.G., M.K., E.C.) and Department of Biostatistics, University of Michigan, Ann Arbor, MI (X.S.).

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Disclosures

Dr Chervin serves on the board of directors for the International Pediatric Sleep Association, and on the advisory board for the nonprofit Pajama Program. He has been an editor for UpToDate and Cambridge University Press. He is named in University of Michigan–owned patents, patents pending, and copyrighted material focused on diagnosis and treatment for sleep apnea and other sleep disorders. He has received royalties from Zansors. The remaining authors have no disclosures to report.

Supplemental Material

Table S1

REFERENCES

1. Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, Nunez CM, Patel SR, Penzel T, Pépin J-L, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med*. 2019;7:687–698. doi: 10.1016/S2213-2600(19)30198-5
2. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, et al. Heart disease and stroke statistics-2021 update: a report from the American Heart Association. *Circulation*. 2021;143:e254–e743. doi: 10.1161/CIR.0000000000000950
3. Seiler A, Camilo M, Korostovtseva L, Haynes AG, Brill AK, Horvath T, Egger M, Bassetti CL. Prevalence of sleep-disordered breathing after stroke and TIA: a meta-analysis. *Neurology*. 2019;92:e648–e654. doi: 10.1212/WNL.0000000000006904
4. McDermott M, Brown DL. Sleep apnea and stroke. *Curr Opin Neurol*. 2020;33:4–9. doi: 10.1097/WCO.0000000000000781
5. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol*. 2013;177:1006–1014. doi: 10.1093/aje/kws342
6. Morgenstern LB, Smith MA, Sánchez BN, Brown DL, Zahuranec DB, Garcia N, Kerber KA, Skolarus LE, Meurer WJ, Burke JF, et al. Persistent ischemic stroke disparities despite declining incidence in Mexican Americans. *Ann Neurol*. 2013;74:778–785. doi: 10.1002/ana.23972
7. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med*. 1999;131:485–491. doi: 10.7326/0003-4819-131-7-199910050-00002
8. ResMed. ApneaLink™ Plus White Paper (D2231-127). 2009. https://www.resmed.com, https://document.resmed.com/en-au/documents/articles/ApneaLink_Plus_White_Paper.pdf. Accessed May 3, 2021.
9. Lisabeth LD, Sánchez BN, Lim D, Chervin RD, Case E, Morgenstern LB, Tower S, Brown DL. Sleep-disordered breathing and poststroke outcomes. *Ann Neurol*. 2019;86:241–250. doi: 10.1002/ana.25515
10. Brill AK, Horvath T, Seiler A, Camilo M, Haynes AG, Ott SR, Egger M, Bassetti CL. CPAP as treatment of sleep apnea after stroke: a meta-analysis of randomized trials. *Neurology*. 2018;90:e1222–e1230. doi: 10.1212/WNL.0000000000005262
11. Schütz SG, Lisabeth LD, Hsu C-W, Kim S, Chervin RD, Brown DL. Central sleep apnea is uncommon after stroke. *Sleep Med*. 2021;77:304–306. doi: 10.1016/j.sleep.2020.08.025
12. Senaratna CV, Perret JL, Matheson MC, Lodge CJ, Lowe AJ, Cassim R, Russell MA, Burgess JA, Hamilton GS, Dharmage SC. Validity of the Berlin questionnaire in detecting obstructive sleep apnea: a systematic review and meta-analysis. *Sleep Med Rev*. 2017;36:116–124. doi: 10.1016/j.smrv.2017.04.001
13. Ramos AR, Guilliam D, Dib SI, Koch S. Race/ethnic differences in obstructive sleep apnea risk in patients with acute ischemic strokes in south Florida. *Sleep Breath*. 2014;18:165–168. doi: 10.1007/s11325-013-0865-9

SUPPLEMENTAL MATERIAL

Table S1. Multivariable models of associations between time and high pre-stroke risk of sleep apnea based on the Berlin Questionnaire.

Characteristic	Adjusted Odds Ratio Estimate (95% Confidence Limits)
Time (year)	1.02 (1.00, 1.05)
Sex (male)	1.29 (1.08, 1.54)
Race/ethnicity (MA:NHW)	0.92 (0.77, 1.10)
Age	1.00 (0.99, 1.00)
Hypertension	4.33 (3.40, 5.52)
Diabetes	1.07 (0.89, 1.29)
Current Tobacco Use	0.99 (0.83, 1.19)
Prior Stroke/Transient Ischemic Attack	1.24 (1.03, 1.50)
Excessive Alcohol	0.95 (0.67, 1.35)
Coronary Artery Disease	1.11 (0.91, 1.34)
High Cholesterol	0.96 (0.80, 1.14)
NIH Stroke Scale Score	1.01 (1.00, 1.02)
Body Mass Index	1.08 (1.06, 1.10)

MA – Mexican American, NHW – Non-Hispanic White, NIH – National Institutes of Health