Association of sleep-related hypoxia with survival in patients with non-small cell lung cancer – the NEOSAS-GFPC study

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Introduction

Sleep-disordered breathing (SDB) and nocturnal hypoxia have been shown to be associated with all-cancer and lung cancer incidence. The prevalence and clinical relevance of SDB in patients with lung cancer remain to be investigated.

Methods

We conducted a prospective, multi-center study within the GFPC network to assess the prevalence of SDB among patients with NSCLC, and the association with quality of life (QOL) and overall survival (OS). Patients underwent home sleep apnea testing (HSAT, ApneaLink, ResMed) and fulfilled sleep and QOL questionnaires, then were followed for 18 months. The diagnosis of SDB was defined as an 3% oxygen desaturation index (3%ODI) of at least 15 events/h.
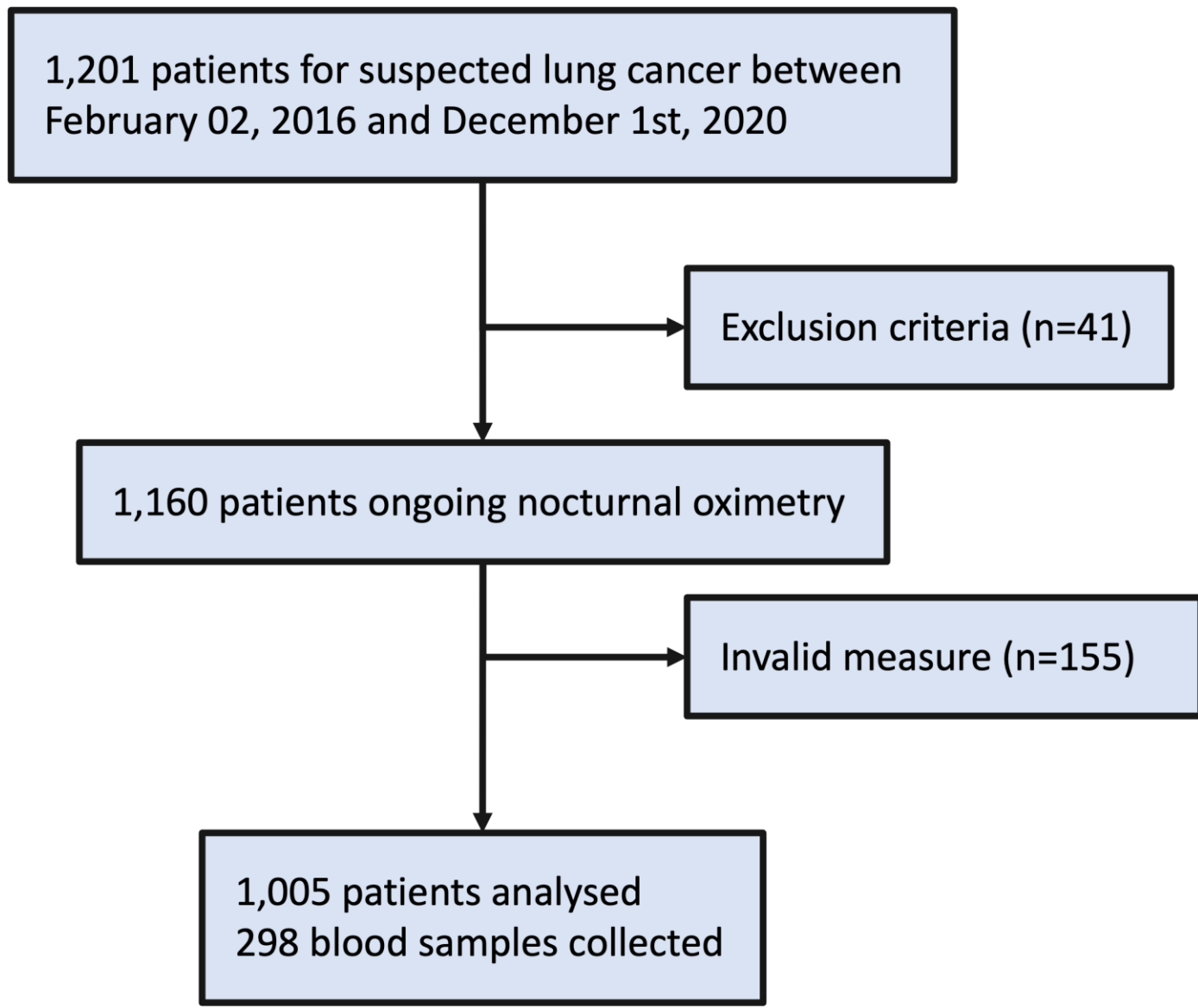
Results

Figure 1 : Study flow-chart

Between February 2016 and December 2020, 1 201 patients with newly diagnosed NSCLC were included. Of 1201 patients, 1001 with valid HSAT were analyzed, 383 of whom (38%) had SDB. Patients with SDB were more frequently male (p<0.0001), had older age (p<0.0001) and higher body mass index (p<0.0001) than those without SDB.

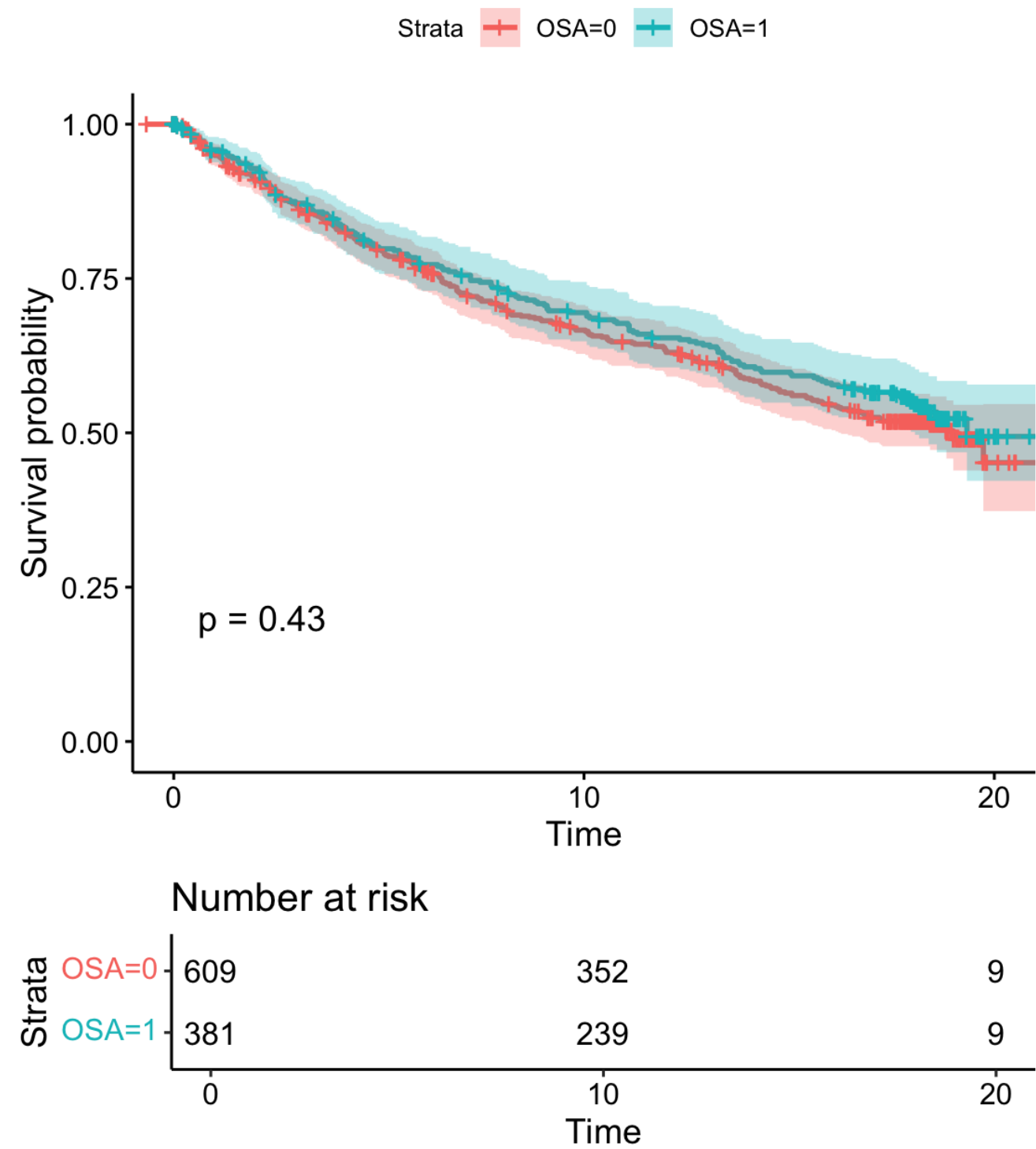Figure 2 : Survival according to SDB – unadjusted (primary outcome) *Kaplan Meier*

Population

Table 1 : Population characteristics according to SDB (primary outcome)

	All (n=1005)	No SDB (n=619)	SDB (n=386)	p-value
Population Characteristics				
Men (%)	709 (71)	405 (66)	304 (79)	**2.844e-06**
Age (SD)	63,67 (9,75)	62,32 (9,64)	65,58 (9,52)	**2.064e-07**
BMI (SD)	24,24 (4,85)	23,58 (4,67)	25,64 (4,81)	**6.263e-11**
Comorbidities				
Hypertension (%)	338 (34)	175 (28)	163 (42)	**3.643e-6**
Stroke (%)	36 (4)	21 (3)	15 (4)	0.6686
Cardiopathy (%)	138 (14)	73 (12)	65 (17)	**0.02139**
Diabetes (%)	144 (14)	74 (12)	70 (18)	**0.005752**
COPD (%)	168 (17)	110 (18)	58 (15)	0.2745
Smoker (ever-smoker or active-smoker) (%)	896 (90)	554 (89)	342 (88)	0.861
Alcohol consumption (%)	447 (45)	277 (45)	170 (44)	0.8928
Cancer characteristics				
Squamous non-small cell lung cancer	257 (26)	139 (22)	118 (30)	**0.003291**
Stage I-II vs III-IV	109 (11)	87 (14)	22 (6)	0.06681
ECOG-PS 0-1 vs 2	860 (86)	532 (86)	328 (84)	0.8731
Sleep Characteristics				
Mean saturation (SD)	91.3 (5.68)	91.7 (6.9)	90.8 (2.69)	**0.003787**
Min saturation (SD)	81 (8.55)	82.4 (9)	78.6 (7.21)	**2.919e-13**
T90 (SD)	30.1 (33.9)	23.9 (31.9)	40.1 (34.6)	**2.516e-13**
<4%	331	271	50	**2.2e-16**
4-36%	345	182	163	
>36%	339	166	173	

There was no association of SDB with QOL excepted for excessive daytime sleepiness (median[IQR] Epworth score: 5.2[3.7] vs 4.7[3.7]; p=0.04), nor with OS. However, patients with marked nocturnal hypoxia (≥36% of sleep recording time with SpO2 <90%, T90)) were at higher risk of death (hazard ratio [95% confidence interval]: 1.37[1.07-1.77]; p=0.01) compared to those with T90<4%) after adjustment for age, gender, BMI, alcohol and tobacco consumption, history of COPD, and NSCLC stage at diagnosis)

Results

Table 2 : Quality of life according to SDB

	All (n=1001)	No SDB (n=618)	SDB (n=383)	p-value
EQ-5D Mobility (SD)	1.30 (0.499)	1.29 (0.502)	1.32 (0.504)	0.4456
EQ-5D Selfcare (SD)	1.11 (0.371)	1.11 (0.363)	1.12 (0.377)	0.6247
EQ-5D Usual activities (SD)	1.37 (0.572)	1.36 (0.577)	1.37 (0.57)	0.7508
EQ-5D Pain/Discomfort (SD)	1.78 (0.621)	1.75 (0.580)	1.79 (0.631)	0.3678
EQ-5D Anxiety/Depression (SD)	1.58 (0.621)	1.56 (0.613)	1.58 (0.617)	0.7584
PSQI (SD)	6.87 (3.99)	6.69 (3.92)	6.88 (4.04)	0.5239
PSQI >= 5 (SD)	661 (0.596)	146 (0.68)	513 (0.68)	0.8935
Pichot (SD)	3.08 (3.19)	2.81 (2.93)	3.14 (3.25)	0.1549
Pichot >=7 (SD)	148 (0.133)	27(0.125)	121(0.159)	0.2212
Epworth (SD)	5.12 (3.77)	4.68 (3.53)	5.26 (3.85)	0.0359
Epworth >=11 (SD)	86 (0.07)	11 (0.05)	75 (0.098)	**0.02808**

Table 3 : Overall survival according to sleep characteristics – unadjusted and adjusted

	Median Survival (months)	No events/No Patients	unadjusted HR (95%CI)	Adjusted HR HR (95%CI)
ODI Tertile 1	18.4	0.4325	Ref	Ref
ODI Tertile 2	19.7	0.4162	0.89371 (0.7070 ; 1.130)	0.9219 (0.7215 ; 1.1781)
ODI Terile 3	19.3	0.4384	0.9339 (0.7409 ; 1.177)	0.9157 (0.7130 ; 1.1761)
T90 Tertile 1	NA	0.3785	Ref	Ref
T90 Tercile 2	19.3	0.4294	1.157 (0.9085 ; 1.473)	1.1708 (0.9092 ; 15078)
T90 Tercile 3	16.8	0.4762	**1.538 (1.2134 ; 1.948)**	**1.4044 (1.0910 ; 1.8078)**

Adjustment factors Age – Gender – BMI – Tobacco – Stage at diagnosis (1-2 vs 3-4) – PS ECOG (0-1 vs 2) – HTA – Stroke – cardiopathy-Diabetes – COPD

Main Finding

SDB is highly prevalent in patients with newly diagnosed NSCLC.

Sustained nocturnal hypoxia estimated through T90 is independently associated with lower OS.