Psychosomatic Medicine and General Practice
Том 10 № 1 (2025)
DOI: 10.26766/pmgp.v10i1.579

Assessment of Obstructive Sleep Apnea severity: Comparison of the Charlson Comorbidity Index and the Functional Comorbidity Index

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Background: Obstructive sleep apnea (OSA) is linked with several comorbidities. Various tools, including the Charlson Comorbidity Index (CCI) and the Functional Comorbidity Index (FCI), are used to assess the influence of comorbidities on the outcomes of chronic diseases. We aimed to compare the predictive ability of the CCI and FCI in assessing how common comorbidities impact the severity of OSA.

Methods: A retrospective study was conducted in a Pneumology Department. Data were collected from medical records of patients diagnosed with OSA. OSA severity was defined by an apnea hypopnea index (AHI) >= 30/h and/or a severe excessive daytime sleepiness. The CCI and the FCI were calculated, correlated to OSA severity predictors and compared.

Results: Severe OSA was noted in 50.6% of patients and severe excessive daytime sleepiness in 17% of patients. The mean CCI was 0.7 ± 0.9, and the mean FCI was 1.6 ± 0.9. The CCI was statistically and weakly correlated to the AHI ($r=0.135$; $p<0.001$) and the Epworth sleepiness scale ($r=0.071$; $p=0.039$). The FCI was statistically and weakly correlated to the AHI ($r=0.131$; $p<0.001$) and strongly correlated to the Epworth sleepiness scale ($r=0.84$; $p=0.014$). For both CCI and FCI, the AUC suggested a model with poor discriminatory ability, not very useful for making predictions of severe OSA, without a statistically significant difference between the two models.

Conclusion: The CCI and FCI were statistically and overall, weakly correlated to OSA severity predictors, without a superiority of one index to another in predicting severe OSA or excessive daytime sleepiness.

Background

Obstructive sleep apnea (OSA) is the most common breathing disorder during sleep, occurring in 2 to 26% of the general population 1.

OSA is characterized by the occurrence during sleep, of repeated, complete or partial, pharyngeal collapse, called apnea or hypopnea, responsible for intermittent hypoxemia and sleep fragmentation, thus daytime sleepiness 2. OSA, by the occurrence of intermittent hypoxemia and reoxygenation, produces oxidative stress, constant sympathetic activation, systemic inflammation and the release of vasoactive mediators 1. Theses reactions cause damage to blood vessel endothelium, leading to atherosclerosis, hypertension, and various cardiovascular diseases 1. Therefore, OSA is a well-known cardiovascular independent risk factor, grafted with a high morbidity and mortality 1. Hence, effective treatment of OSA may represent an important target for improving cardiometabolic risk 2.

OSA is a condition recognized to be associated with multiple chronic comorbidities that can impact physical functional status 3. Comorbidities can influence the evolving course, the prognosis, and the management outcome of OSA 4. Thus, optimally managing other comorbidities, tend to have better overall OSA treatment outcome 4.

To amount for multiple comorbidities and measure their related prognosis, an index is often used for studying their mortality effect, including life-threatening conditions 4.

Numerous tools are used to assess the impact of comorbidities on chronic diseases outcome 3. For example, Charlson comorbidity index (CCI), being especially developed to predict long-term mortality, is currently a reliable, sensitive, well-validated and widely-used tool to measure prognostic comorbidities in various chronic conditions 5. Thus, the CCI, firstly reflects the patients' clinical profile, and secondly defines the main prognostic particularities, differing patients sharing the same disease, from each other, according to their baseline conditions and medical background, opening options for a more personalized management 5.

A new tool, Functional comorbidity index (FCI), developed by Groll et al 6 with physical function as the outcome, includes common comorbidities influencing daily life and function regardless of mortality risk 4. The FCI, being specifically designated in order to determine the comorbidities' effect on the physical functioning subscale of the Medical Outcomes Short Form-36 Health Survey (SF-36), focuses mainly on the quality of life 3.

These two indices might be appropriate to adjust for baseline differences in comorbidities when assessing mortality and functional outcomes in OSA. The aim of this study was to determine the predictability of the CCI and the FCI in evaluating the impact of common comorbidities on OSA severity and to compare the association between OSA severity and the two indices.

Methods

Study Design and Sample

This was a retrospective, single-center, and observational study, conducted in the Sleep center of the Pneumology Department D of Abderahmen Mami Hospital in Tunisia. Data were collected from medical records of patients seen between 2014 and 2024, diagnosed with OSA by a ventilatory polygraphy or polysomnography, performed either at hospital or at home.

This study was conducted in accordance with ethical recommendations. All data collected in this

study are confidential and anonymous. All procedures were performed in compliance with relevant laws and institutional guidelines and have been approved by the local hospital ethics committee.

From 4011 revised records of patients having had a ventilatory polygraphy or polysomnography, 2039 were diagnosed with OSA. We included patients of at least 18 years of age, diagnosed for the first time in our department with OSA by a diagnostic ventilatory polygraphy or a polysomnography, based on the American Academy of Sleep Medicine (AASM) accredited scoring standards, defined by apnea hypopnea index (AHI) of five or more events per hour of sleep 7. We did not include patients below 18 years of age, with an associated obesity hypoventilation syndrome, with another non-respiratory sleep disorder (narcolepsy, restless legs syndrome, hypersomnia, …), with neurological or muscular pathologies (myopathy, encephalopathy, …), with central sleep apnea, or under neuroleptic drugs. Excluded from the study, patients with missing data records.

Data Collection and Applied Definitions

Data were retrospectively extracted by the medical staff in 2024, from medical records of patients seen for the ten years prior to study enrollment, between 2014 and Juin 2024. Patients were diagnosed with OSA by a ventilatory polygraphy or polysomnography, performed either at hospital or at home.

For each patient, the clinical data recorded were demographic characteristics (age, gender, …), lifestyle habits (smoking, stimulants, …), personal history, nocturnal and diurnal symptoms, weight, height, and body mass index (BMI) 8. The snoring, tiredness, observed apnea, high blood pressure, age, neck circumference, and male gender (STOP-Bang) questionnaire, consisting of eight yes/no items related to the clinical OSA features, as a specifically reliable screening tool, was assessed 9. The total score ranges from 0 to 8, classifying patients for OSA risk, with a sensitivity of STOP-Bang score ≥ 3 to detect moderate to severe OSA 9. Daytime sleepiness was measured by the Epworth sleepiness scale (ESS) 10, a questionnaire that was filled out by the medical staff during the first consultation, extracted from patients’ charts. This scale comprises eight situations that can be encountered in everyday life, and patients rate their propensity to doze off or fall asleep in each of these situations, assigning a score from 0 (never dozing off) to 3 (high likelihood of falling asleep) 10. The sum of the eight ratings results in a score ranging from 0 to 24, with a value above 10 considered abnormal 10. Tiredness was measured using the Pichot's Fatigue scale, a practical scale consisting of 8 questions, scored progressively from 0 (not at all) to 4 (extremely) 11. The summed score ranged from 0 to 32 and a total score above 22 revealed excessive fatigue 11.

Polygraphic data collected from the finalized ventilatory polygraphy or polysomnography report, were AHI, dorsal and non-dorsal AHI, oxygen desaturation index (ODI), mean and minimum pulse oxygen saturation (SpO2) during sleep, the mean apnea and hypopnea duration, and the total recording time with SpO2 <90% and <88%.

The level of OSA severity was mainly judged based on the frequency of occurrence of abnormal respiratory events and the extent of daytime sleepiness after exclusion of another cause of sleepiness 7. Based on the AHI, mild OSA was defined by AHI between 5 and 15 per hour, moderate OSA by AHI between 15 and 30 per hour, and severe OSA by AHI greater than or equal 30 per hour 7. A severe excessive daytime sleepiness was defined by an ESS >16 10.

In addition to the AHI and the ESS, other clinical and polygraphic parameters were considered as predictors of OSA severity, such as age, Stop Bang score, BMI, Pichot’s fatigue scale, ODI, mean and minimum SpO2 during sleep, total recording time with SpO2 below 90% and 88%, and mean apnea hypopnea duration 9 12 13 14 15.

The CCI and the FCI were calculated afterwards by the study investigator, from the retrieved patients’ charts, providing information about comorbidities and their severity.

The CCI is a weighted index that was developed and validated prospectively, in longitudinal studies with a 559 patients' cohort, by Charlson et al. 16. This 19-item index classify different comorbid conditions based on their seriousness and mortality risk predictability in an increased level with a cumulative effect 16. Thus, the separate conditions were scored from one to six, according to a severity weigh assignment, summed to a final CCI, a continuous variable ranging from 0 to 37 4. Age was also prospectively proved to be associated with mortality, thus was considered a mortality predictor further aggravating patients' disease prognosis 16. The age-adjusted CCI (A-CCI) was calculated by summing the weighted comorbidities and age of each patient. The CCI and A-CCI items and scoring are listed in ***figure 1*** 17. Based on the CCI score, the severity of comorbidities was categorized into three grades: mild, with CCI scores of 1-2; moderate, with CCI scores of 3-4; and severe, with CCI scores ≥5 18.

Figure 1: The Charlson comorbidity index 19 items and age-adjusted scoring

Score	Comorbid Condition
1	Myocardial infarction Congestive heart failure Cerebral vascular disease Peripheral vascular disease Dementia Chronic obstructive pulmonary disease Connective tissue disease Peptic ulcer disease Mild liver disease
2	Diabetes Hemiplegia Moderate/severe renal disease Diabetes with end-organ damage Any solid tumor Leukemia Lymphoma
3	Moderate/severe liver disease
6	Metastatic solid tumor AIDS
Age (y)	
41–50	1 point
51–60	2 points
61–70	3 points
≥71	4 points

The FCI was developed to predict physical functional status burden measured on the SF-36, using comorbidity data 4 19. The FCI was developed and validated in 2005 by Groll et al. 6 using two databases; one over 9000 randomly sampled Canadian adults, and one over 28000 US adults seeking treatment for spine diseases, with the SF-36 physical function (daily living activities) as the primary outcome 4. ***Figure 2*** summarizes the 18 items of the FCI 19. Each item is scored with one,

summed to a final FCI, a continuous variable ranging from 0 to 18 19.

Figure 2: The Functional comorbidity index 18-items

	Comorbidity
1	Arthritis (rheumatoid and osteoarthritis)
2	Osteoporosis
3	Asthma
4	Chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), or emphysema
5	Angina
6	Congestive heart failure (or heart disease)
7	Heart attack (myocardial infarction)
8	Neurological disease (e.g., multiple sclerosis or Parkinson's disease)
9	Stroke or transient ischemic attack (TIA)
10	Peripheral vascular disease
11	Diabetes types I and II
12	Upper gastrointestinal disease (e.g., ulcer, hernia, reflux)
13	Depression
14	Anxiety or panic disorders
15	Visual impairment (e.g., cataracts, glaucoma, macular degeneration)
16	Hearing impairment (i.e., very hard of hearing, even with hearing aids)
17	Degenerative disc disease (e.g., back disease, spinal stenosis, or severe chronic back pain)
18	Obesity and/or body mass index (BMI) > 30

Statistical Analysis

Descriptive analysis of variables was expressed as median ± standard deviation, mean or percentage (%).

To compare percentages, the chi-square test was used on independent series, and in case of its non-validity, the two-tailed Fisher test was used. To compare means between two independent samples, the Student's T-test was used. To compare means for non-dichotomous categorical variables, the ANOVA test was used when their distribution was normal, and the non-parametric Kruskal-Wallis test in other cases.

To compare the correlation between the CCI and the FCI with the severity of OSA:

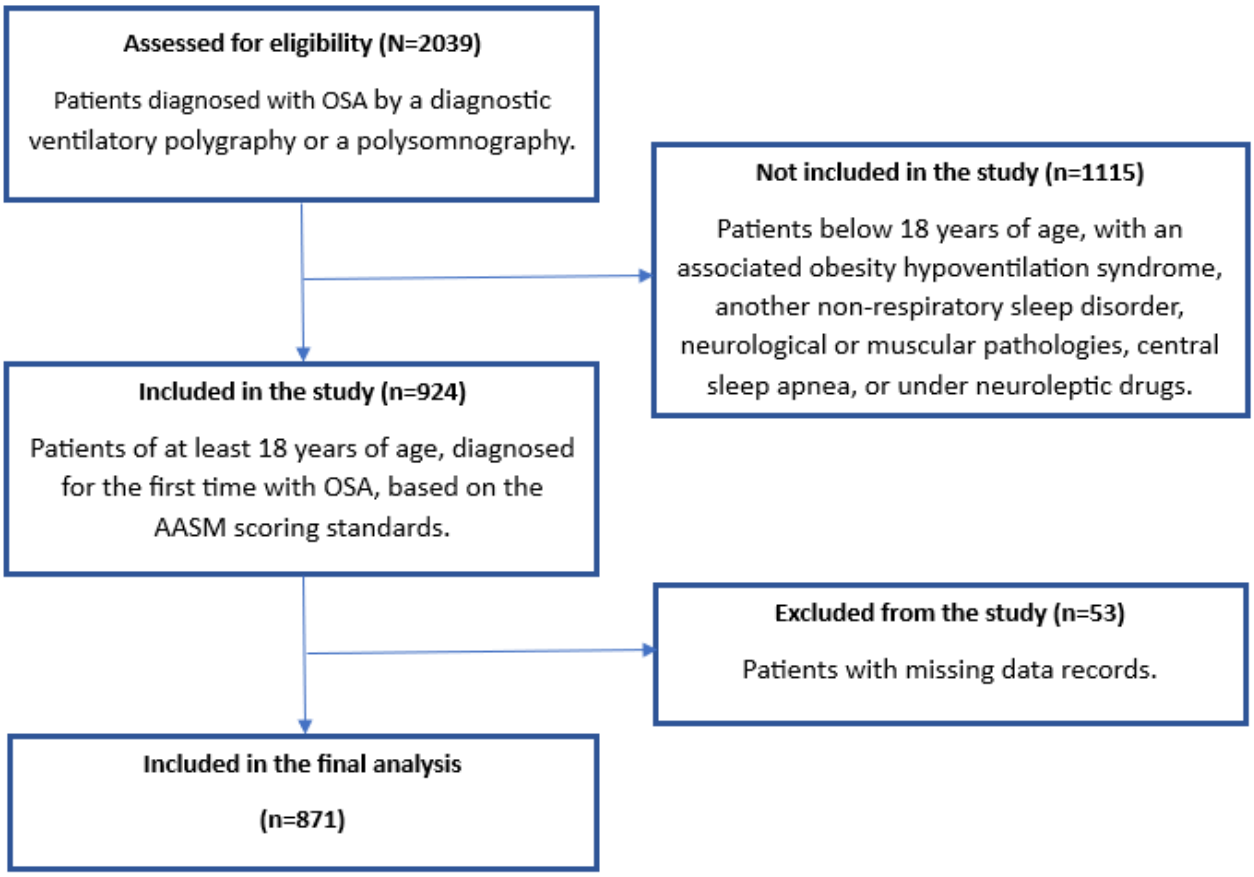
- We calculated correlations between CCI and OSA severity predictors, then between FCI and OSA severity predictors. Correlations were studied using the Pearson or Spearman test, depending on the normality of the distribution of variables. If CCI, FCI and OSA severity scores are continuous variables and follow a normal distribution, the Pearson correlation coefficient will be used. If the data do not follow a normal distribution, the Spearman's correlation can be used. According to the correlation coefficient r, the correlation was considered strong when $r>0.5$, average for r between 0.3 and 0.4, and weak when $r<0.3$.

- We tested the strength of the two correlations, using the Receiver Operating Characteristic curve (ROC curve), to assess the relative performance of models in a classification setting based on the correlations. The two ROC curves of the two correlations were compared by the Area Under the Curve (AUC) for each ROC curve’s performance. The AUC provides a summary measure of the ROC curve’s performance: higher AUC values indicate better predictive performance. An AUC of 0.5 indicates a total absence of discriminating ability in this context, thus the model is null and performs no better than random chance. A statistical test was performed to determine if the difference in AUC values between the two ROC curves is significant.

For all statistical tests, the significance threshold was set at 0.05 (5%), thus a p-value <0.05 was considered a statistically significant correlation different from zero. Data were entered and analyzed using SPSS software version 26.0.

Results

From 4011 revised records of patients having had a ventilatory polygraphy or polysomnography, 2039 were diagnosed with OSA, from whom 871 patients were included in the final analysis. ***Figure 3*** presents the flowchart of the study.



The study population characteristics were summarized in ***Table 1***. The patients were not heterogeneously distributed according to OSA severity, they were mostly severe with 50.6% of patients presented with AHI >=30 per hour, 17.8% of patients with moderate OSA, and 31.6% patients with mild OSA. The mean AHI was 48.2/h in severe OSA patients. Severe excessive daytime sleepiness was noted in 17% of patients, with a mean ESS at 11.3 ± 5.6.

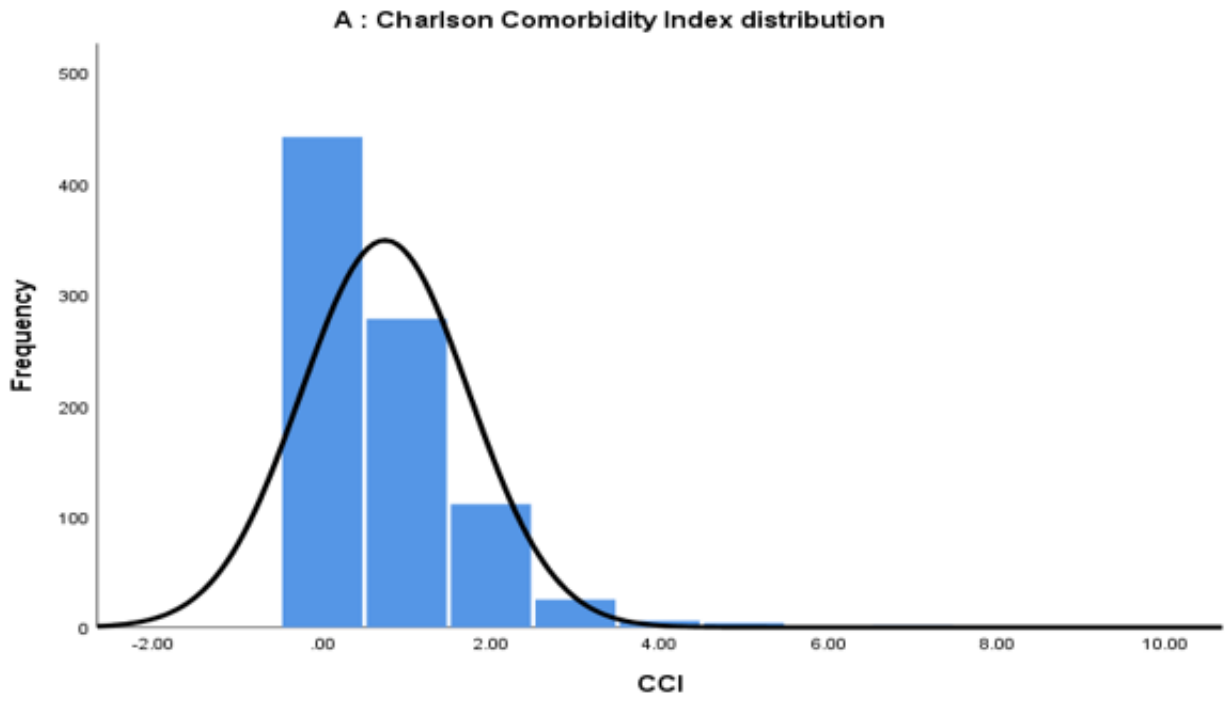
Table 1: The cohort characteristics

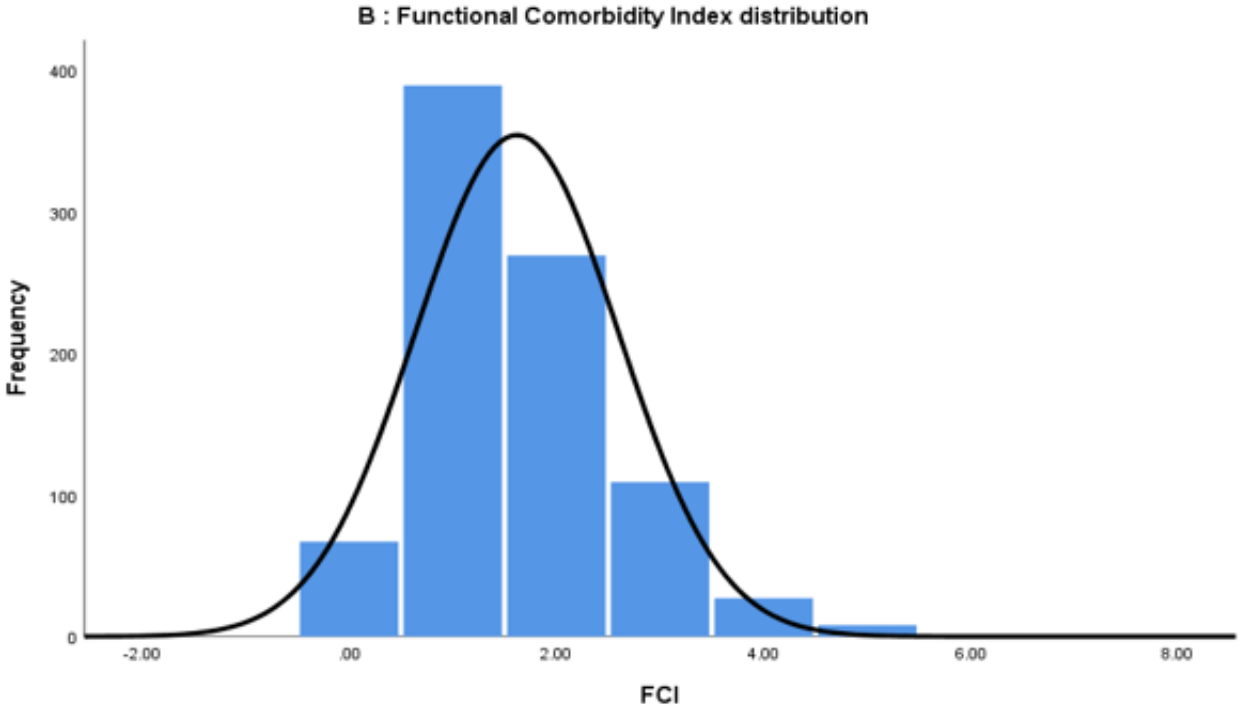
Characteristics	Mean	Standard deviation	Range
Age (years)	57.05	11.9	18 – 96
Female (%)	72.3		
Smoking (%)	18.9		
Body Mass Index (kg/m2)	36.5	7.3	21.4 – 69
Stop Bang score (0-8)	4.3	1.8	0 – 8
Epworth Sleepiness Scale (0-24)	10.6	5.8	0 – 24
Pichot’s Fatigue scale (0-32)	17.2	8.4	0 – 32
Apnea Hypopnea Index (events/hour)	36.5	23.19	5.1 – 163
Oxygen desaturation index (events/hour)	30.5	23.3	0 – 164
Mean pulse oxygen saturation during sleep (%)	93	6.2	50 – 98.5
Minimum pulse oxygen	77.3	10.5	40 – 94.7

saturation during sleep (%)			
Total recording time with saturation <90% (%)	14.7	22.4	0 – 99.8
Total recording time with saturation <88% (%)	10.1	17.4	0 – 99.6
Mean apnea duration (seconds)	18.5	8	0 – 82.1
Mean hypopnea duration (seconds)	23.3	5.9	0 – 55.9
Charlson comorbidity index (0-37)	0.7	0.9	0 – 8
Age-adjusted Charlson comorbidity index (0-41)	2.1	1.6	0 – 10
Functional comorbidity index (0-18)	1.6	0.9	0 – 6

The CCI scores were less widely distributed than the FCI scores. Most patients had less than one comorbidities in the CCI compared to one comorbidity in the FCI (***Figure 4***).

Figure 4: Histograms present the cohort patients' distribution according to each Index score. A: Charlson comorbidity Index (CCI) histogram, mean = 0.7±0.9; range observed = 0–8 (potential range 0–37). B: Functional comorbidity Index (FCI) histogram, mean = 2.1±1.6; range observed = 0–10 (potential range 0–18).





The CCI and the FCI were statistically and strongly correlated (r=0.833; p<0.001).

Table 2showed the correlations between CCI and OSA severity parameters, then between FCI and OSA severity parameters. The data did not follow a normal distribution; thus, the Spearman's correlation was used. Both indices CCI et FCI were statistically correlated to the age, Stop Bang score, the ESS, the Pichot’s fatigue scale, the AHI, the ODI, the mean SpO2 during sleep, the minimum SpO2 during sleep, and the total recording time with SpO2 <90% and 88%. Compared to CCI, only FCI was statistically correlated to the BMI. With both CCI and FCI, no statistically

significant correlation was found with the mean apnea duration. All correlations were weak with r below 0.3, except for the FCI and the ESS (r=0.84; p=0.014).

Table 2: Correlations between the Charlson comorbidity index, the Functional comorbidity index, and obstructive sleep apnea severity predictors

OSA severity predictors	Charlson comorbidity index		Functional comorbidity index	
		r	***p***	**r**
Age (years)	0.217	***<0.001***	0.182	***<0.001***
Stop Bang score (0-8)	0.183	***0.001***	0.209	***<0.001***
Body mass index (kg/m2)	0.062	*0.07*	0.248	***<0.001***
Epworth Sleepiness Scale (0-24)	0.071	***0.039***	**0.84**	***0.014***
Pichot's Fatigue scale (0-32)	0.18	***<0.001***	0.223	***<0.001***
Apnea Hypopnea Index (events/hour)	0.135	***<0.001***	0.131	***<0.001***
Oxygen desaturation index (events/hour)	0.145	***<0.001***	0.140	***<0.001***
Mean pulse oxygen saturation during sleep (%)	-0.103	***0.003***	-0.161	***<0.001***
Minimum pulse oxygen saturation during sleep (%)	-0.096	***0.005***	-0.111	***0.001***
Total recording time with saturation <90% (%)	0.126	***<0.001***	0.155	***<0.001***
Total recording time with saturation <88% (%)	0.09	***0.022***	0.117	***0.003***
Mean apnea duration (sec)	0.068	*0.074*	0.016	*0.663*

OSA : Obstructive sleep apnea ; sec : seconds

Table 3compared the two correlations between CCI and OSA severity main predictors and between FCI and OSA severity main predictors with ROC curves. For both CCI and FCI, the AUC was between 0.5 and 0.7, suggesting a model with poor discriminatory ability, better than random guessing but not very useful for making predictions of severe OSA or severe excessive daytime sleepiness. The 95% confidence intervals for the two ROC curves overlapped suggesting that there is no difference between the AUCs of the two models, thus there is no superiority of one index to another in predicting severe OSA or severe excessive daytime sleepiness.

Table 3: Comparison of the predictability of obstructive sleep apnea severity between the Charlson comorbidity index and the Functional comorbidity index with ROC curves

OSA severity predictors	Comorbidity indices	AUC	*p*	CI 95%
Severe OSA	CCI	0.566	***0.001***	[0.528; 0.604]

(AHI>=30/h)		FCI	0.569	***<0.001***
Severe excessive daytime sleepiness (ESS>16)	CCI	0.532	*0.228*	[0.480; 0.583]
		FCI	0.545	*0.084*

AHI: Apnea hypopnea index; AUC: Area under the curve; CCI: Charlson comorbidity index; CI: Confidence interval; ESS: Epworth sleepiness scale; FCI: Functional comorbidity index; OSA: Obstructive sleep apnea; p: p-value

Discussion

Data of 871 OSA patients were retrospectively collected, and used to calculate two comorbidity indices; the CCI and the FCI.

Male gender is considered as an OSA risk factor, acknowledging the anatomic differences in airway collapsibility and fat distribution, and the protective effect of female hormones 20. Contrary to the literature which has long considered OSA as a predominantly male-related disease, female predominance was highlighted in our Tunisian cohort (72.3%) 21. Other physiological features occurring in females with OSA related to genetic or ethnic risk factors, are yet to be established and remain unanswered 21. The advanced age in our cohort compared to Levin at al. 4 cohort, may partially explain this gender distribution, as the prevalence of OSA increases with age, especially in menopausal women 21.

OSA is a condition highly associated with multiple comorbidities, impacting quality of life and increasing cardiovascular morbidity and mortality 22. Its impact is directly related to its degree of severity, as it has long been reported that the AHI is associated with serious coexisting conditions 22. Thus, an early diagnosis and management of severe OSA may reduce its impact 23. Other more rapid means than ventilatory polygraphy or polysomnography are needed to select the most severe and urgent patients to diagnose and treat 24.

The US Preventative Services Task Force states that the current evidence is insufficient to assess the balance of benefits and harms of screening all asymptomatic adult patients for OSA 25. Whereas, the AASM recommends screening certain asymptomatic populations at high-risk of OSA, including those with atrial fibrillation, resistant hypertension, congestive heart failure, obesity, diabetes mellitus, nocturnal dysrhythmias, pulmonary hypertension, high risk driving populations, and preoperative patients for bariatric surgery, using validated questionnaires 20. The Stop Bang score, Berlin questionnaire, and ESS are commonly used 24. But, to this day, to the best of authors' knowledge, no single tool that met its criteria for clinical validity and feasibility has been identified 20.

Therefore, finding other suitable tools to assess comorbid conditions may be useful to predict OSA severity.

The CCI and FCI are widely used means to assess the impact of comorbidities on various chronic diseases outcome 3. And this paper compared these two comorbidity indices to determine the more predictable and strongly associated to OSA severity, thus the more suitable tool to use to prioritize diagnosing and treating the patients with the most severe and urgent conditions.

Our results indicated that the FCI, compared to the CCI, was more strongly correlated to the ESS and the Pichot's fatigue scale, thus proved to be more correlated to excessive daytime sleepiness and fatigue, known as OSA common symptoms 24. In fact, the FCI is known to be more closely related to the impact of OSA on daily living and physical function 3. Therefore, the present study highlighted that the FCI may show stronger correlation with OSA severity, if focused on how OSA affects the patient's daily functioning. On the contrary, the CCI, as known to be more reflective of the mortality risk, is predicted to be more correlated to OSA severity in terms of cardiovascular and metabolic comorbidities 18. Our results were inconsistent with those reported in the literature as the FCI, compared to the CCI, was more strongly correlated to the Stop Bang score and the BMI. This can be explained by the fact that the FCI included several conditions such as cardiovascular disease, stroke, and diabetes, as included in the CCI 4 18. Accordingly, both indices could provide valuable information depending on the specific aspect of OSA and comorbidities being evaluated.

In the present study, the CCI and FCI showed no difference in predicting severe OSA or severe excessive daytime sleepiness.

Supporting our statement, Rundell et al. 26 compared the CCI and FCI for older adults with back pain and reported that all indices performed similarly in predicting outcomes without an advantage to using one index over another.

On the other hand, in another study, the CCI and FCI were compared in terms of their predictability of health status with the SF-36 as the outcome in OSA patients, supporting the FCI as a more robust predictor than the CCI 4. In accordance, Groll et al. 27 stated that the FCI compared to the CCI is a better method of measuring comorbidity with physical function as the outcome in acute respiratory distress syndrome patients.

Conclusion

In conclusion, the CCI and FCI were overall statistically correlated to OSA severity predictors, appearing as promising tools for detecting the most severe cases, to be prioritized for rapid diagnosis and management, without a superiority of one index over another in predicting severe OSA or severe excessive daytime sleepiness. There is still a need to develop better risk adjustment models of standard comorbidities and functional outcomes to improve prediction of OSA severity.

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