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Quality of Life in Moderate-Severe OSA Patients from North-Eastern Romania

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Abstract

Obstructive sleep apnea (OSA) is the most common type of sleep disordered breathing, with a significant impact on health-related quality of life (HR-QoL). Continuous positive airway pressure (CPAP) is the gold-standard treatment for moderate-severe OSA, but is associated with poor patient compliance (due to financial issues and frequent side effects). The purpose of this study is to evaluate HR-QoL among patients with moderate-severe OSA from North-Eastern Romania, at baseline and after 2 months of CPAP. 75 patients were initially included in our study but only 59 subjects returned for a second evaluation. HR-QoL was assessed using the European Quality of Life 5 Domain questionnaire (EQ-5D-5L). OSA has a significant impact on quality of life in our group, with an average EQ-5D-5L index of 0.70±0.27 and an EQ-5D-5L Visual Analogue Scale (VAS) of 63.71±17.74%. Short-term CPAP use was associated with a statistically significant improvement in Epworth Sleepiness Scale ($\Delta = 4.44$, $p < 0.0000001$), EQ-5D-5L index ($\Delta = 0.1$, $p=0.0008$) and EQ-5D-5L VAS ($\Delta = 9.38\%$, $p=0.00002$). All patients with a high income (> 4000 lei/month) decided to continue using the device, while the decision not to continue CPAP was significantly more frequent among patients with a low income (< 1000 lei /month - 52.63% versus 21.21%, $p=0.01$). Our results suggest that income level significantly influences CPAP compliance.

Keywords: obstructive sleep apnea, CPAP, quality of life, EQ-5D-5L, Epworth Sleepiness Scale, social status, social life.

Introduction

Obstructive sleep apnea (OSA) is the most common form of sleep disordered breathing, characterized by recurrent nocturnal hypoxic episodes due to partial or complete upper airway collapse (Hoyos *et al*., 2012). Although OSA prevalence was previously thought to be up to 4% (Young *et al*., 1993), due to the current rise in obesity and to the recent changes regarding OSA diagnosis criteria, it is now estimated that 10-49.7% of adults suffer from different degrees of sleep apnea (Lorenzi-Filho, Almeida and Strollo, 2017). OSA is a recognized risk factor for cardio-metabolic and cerebro-vascular disease (Hoyos *et al*., 2012) and is also

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associated with a significant reduction in general quality of life (D'Ambrosio, Bowman and Mohsenin, 1999; Chakravorty, Cayton and Szczepura, 2002; Kuhn, Schwarz, Bratton, Rossi and Kohler, 2017).

The world health organization (WHO, 2019) broadly defines quality of life (QoL) as "the individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations and concerns" (WHO, 2019). The concept of health-related QoL (HR-QoL) was developed in order to minimize the effect of social status, environment and other confounding factors on medical analysis.

The European Quality of Life Questionnaire (EuroQoL), Short Form 36 (SF-36), Patient generated index (PGI) and Nottingham Health Profile (NHF) are the most common generic instruments that evaluate HR-QoL, both generally and within certain domains (Dutt and Chaudhry, 2016). Generic questionnaires are less sensitive compared to disease specific instruments such as Functional Outcomes of Sleep Questionnaire, Obstructive Sleep Apnea Patient-Oriented Severity Index and Sleep Apnea Quality Of Life Index (Dutt & Chaudhry, 2016). However, generic questionnaires allow a comparison between different populations and medical conditions, being considered more suitable for research. The European Quality of Life 5 Domain questionnaire (EQ-5D-5L) was developed in 1990 and has become one of the most widely used tools for the assessment of health-related QoL. The first part of the EQ-5D questionnaire evaluates 5 health-related domains (mobility, self-care, usual activities, pain/discomfort and symptoms of anxiety/depression) on a scale of 1 to 5 (no problems, slight, moderate, severe or extreme problems, respectively). In the second part of the questionnaire the patient chooses a self-assessed level of health, using a visual analogue scale labeled from 0 to 100 (the worst and the best health status that one can imagine, respectively). Utility indices facilitate the analysis of HR-QoL by providing a general summary score of the analyzed dimensions, but they are influenced by several factors, including age, sex and, to some degree, socioeconomic status (Schmidlin *et al*., 2010).

CPAP is the gold-standard therapy for moderate-severe OSA (Kuhn *et al.*, 2017), with clear metabolic and cardiovascular benefits (Montesi, Edwards, Malhotra and Bakker, 2012), but also improved overall cognitive performance (Wang *et al*., 2019). Since chronic sleep disruption is also associated with neuropsychiatric consequences affecting patients both professionally and personally (Jing, Huang, Cui and Shen, 2008; Wang *et al*., 2019), an in-depth analysis of CPAP effectiveness must include subjective outcomes such as health-related quality of life. Although a recent review concluded that CPAP use increases QoL in moderate-severe OSA (Dutt and Chaudhry, 2016), previous meta-analyses have yielded conflicting results (Jing *et al*., 2008; Okuno *et al*., 2014). The purpose of this study is to investigate HR-QoL using the EQ-5D-5L among Romanian patients with moderate-severe OSA, at baseline and after 2 months of CPAP.

Methodology

Our study included 75 CPAP naïve patients with moderate-severe OSA (apnea-hypopnea index ≥ 15). OSA was diagnosed using ambulatory or in-hospital 6-channel cardio-respiratory polygraphy (Philips Respironics Alice Night One or DeVilbiss Porti 7). The recordings were manually interpreted, according to the 3rd International Classification of Sleep Disorders (Sateia, 2014). CPAP effective pressure was automatically determined in the sleep laboratory (Philips Respironics DreamStation Auto CPAP or Resmed Airsense 10 Autoset). All subjects signed an informed consent prior to study enrollment and were offered a free 2 months CPAP therapy trial. 16 patients were intolerant to CPAP or did not return for reevaluation. The EQ-5D-5L and Epworth Sleepiness Scale (ESS) questionnaires were completed before and after 2 months CPAP, in the presence of a certified health care provider who was able to offer supplementary information, when necessary. In the absence of a Romanian value set (Olariu *et al*., 2019), we chose to compute the Index Value using the UK crosswalk value sets (similar to other analysis of Romanian patients (Rencz *et al*., 2016)), using the calculator provided by the EQ-5D official website (available at https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/crosswalk-index-value-calculator/). The 59 patients who were present for reevaluation were contacted via telephone after 1 month to inquire whether they decided to continue CPAP therapy.

Variables are reported by means and SD or percentages, as appropriate. Student's t test was used to compare moderate and severe OSA subgroups. The decision to continue CPAP in relation with income level was analyzed using Z test. Spearman's correlations were computed between apnea severity (AHI), Epworth score results, EQ-5D-5L utility index, age and income. A p value <0.05 was considered statistically significant.

Results

Our analysis included 75 subjects: 30 and 45 patients with moderate and severe OSA, respectively, aged 36-79 years old (58.40±8.89) (*Table 1*). We found no significant differences regarding age, income, the EQ-5D-5L index and VAS between moderate and severe OSA. Although the overall Epworth score was similar in the two apnea severity subgroups, patients with severe apnea were more likely to doze or fall asleep while "sitting inactive in a public place (theatre or a meeting)" and while "sitting quietly after lunch without alcohol" (*Table 1*). Cardio-metabolic comorbidities were highly prevalent in our study group, with 96%, 77.33% and 32% of patients suffering from hypertension, obesity and type 2 diabetes, respectively.

Table 1: Descriptive statistics of our study group (N=75 patients)

	Moderate-severe OSA	Moderate OSA	Severe OSA	P
Age	58.40±8.89	58.27±8.71	58.49±9.09	0.91
Income	1899.17±1438.20	1836.8±1490.29	1939.41±1427.06	0.80
AHI	39.94±19.87	21.82±4.16	52.01±16.73	< 0.00001
EQ-5D-5L Index	0.70±0.27	0.72±0.28	0.70±0.27	0.75
EQ-5D-5L VAS	63.71±17.74	62.57±18.50	64.52±17.35	0.64
Epworth Score	8.14±5.45	6.97±4.54	8.98±5.92	0.12
Sitting and reading	1.49±1.21	1.37±1.22	1.57±1.21	0.48
Watching TV	1.83±1.06	1.73±1.17	1.90±0.98	0.50
Sitting inactive in a public place (theatre or a meeting)	0.65±1.06	0.30±0.65	0.90±1.23	0.016
As a passenger in a car for an hour without a break	0.75±1.08	0.67±0.88	0.81±1.21	0.58
Lying down to rest in the afternoon when circumstances permit	2.06±1.09	1.97±1.10	2.12±1.09	0.56
Sitting and talking to someone	0.19±0.55	0.13±0.43	0.24±0.62	0.42
Sitting quietly after lunch without alcohol	1.06±1.14	0.73±1.08	1.29±1.13	0.04
In a car, while stopped for a few minutes in traffic	0.08±0.33	0.10±0.40	0.07±0.26	0.71

Health index value was not significantly correlated with apnea severity (r=-0.08, p=0.49) or income (r=0.12, p=0.40). Self-assessed health status according to the VAS was not significantly correlated with income (r=0.26; p=0.06) or apnea severity (r=0.16; p=0.16). We found no statistically significant correlations between AHI and overall ESS score (r=0.19; p=0.11).

Table 2: EQ-5D-5L and Epworth Sleepiness Scale results, before and after 2 months CPAP (N=59 patients)

	Before CPAP	After CPAP	P
EQ-5D-5L Index	0.72±0.26	0.82±0.21	0.0008
EQ-5D-5L VAS	66.83±17.77	76.21±15.34	0.00002
Epworth Score	8.41±5.58	3.97±3.70	<0.0000001
Sitting and reading	1.64±01.22	0.86±1.02	0.00005
Watching TV	1.86±1.08	0.98±0.96	0.000003
Sitting inactive in a public place (theatre or a meeting)	0.66±1.04	0.26±0.55	0.002
As a passenger in a car for an hour without a break	0.79±1.14	0.29±0.68	0.002
Lying down to rest in the afternoon when circumstances permit	2.05±1.13	1.03±1.06	<0.0000001
Sitting and talking to someone	0.21±0.59	0.07±0.26	0.11
Sitting quietly after lunch without alcohol	1.10±1.13	0.41±0.70	0.00005
In a car, while stopped for a few minutes in traffic	0.09±0.24	0.05±0.29	0.57

Average CPAP use in our group was 240.9±133.38 minutes/night. EQ-5D-5L index and VAS significantly improved after 2 months CPAP (p=0.0008 and p=0.00002, respectively) (*Table 2*). Overall Epworth score decreased after CPAP, with statistically significant improvements in all domains except for "sitting and talking to someone" and "in a car, while stopped for a few minutes in traffic" *(Table 2)*.

Table 3: Income level in relation with the decision to continue CPAP use or not

Income level	Continues CPAP treatment			
	YES	NO		
	%	%	Z test	p
< 1000	21.21	52.63	2.33	0.01
1000-1499	12.12	10.53	0.17	0.43
1500-1999	24.24	15.79	0.72	0.24
2000-2499	6.06	10.53	0.58	0.28
2500-2999	9.09	5.26	0.50	0.31
3000-3499	6.06	5.26	0.12	0.45
3500-3999	0	0	/	/
4000-4499	3.03	0	0.77	0.22
4500-4999	3.03	0	0.77	0.22
5000-5499	6.06	0	1.09	0.14
5500-5999	0	0	0	0
6000-6499	6.06	0	1.09	0.14
6500-6999	3.03	0	0.77	0.22

The decision not to continue CPAP was more frequent among individuals with a low income (< 1000 lei: 52.63% versus 21.21%, p=0.01) (*Table 3*). All patients with an income > 4000 lei decided to continue CPAP (21.21% versus 0%, p=0.015). There was no significant difference regarding the decision to continue the treatment among patients with an income between 1000 and 3500 lei.

Discussion

HR-QoL reflects the individual's perception concerning the impact of disease on every-day life. Although HR-QoL *per se* is a subjective concept, researchers have attempted to transform QoL into a quantifiable, research-appropriate parameter by developing different questionnaires. Although generic instruments are less sensitive than disease-specific questionnaires, the former are preferred if the patient is suffering from multiple medical conditions (as was the case in our study) (Dutt and Chaudhry, 2016).

Similar to other reports, the average age in our study group was 58.40±8.89 years old, with a marked prevalence of OSA among male subjects (M:F ratio – 57:18) (D'Ambrosio *et al*., 1999). Our results show that OSA has an important impact on HR-QoL in the Romanian population, with an average EQ-5D-5L index similar to that of Romanian patients with stable coronary artery disease (0.72 versus 0.75)(De Smedt *et al*., 2016). Four other studies analyzed HR-QoL among CPAP naïve OSA patients, and reported only a slightly higher EQ-5D utility index than ours (0,73 - 0,79) (Chakravorty *et al*., 2002; Jenkinson, Stradling and Petersen, 1997; Mar, Rueda, Durán-Cantolla, Schechter and Chilcott, 2003; Jenkinson, Stradling and Petersen, 1998). However, another study (Schmidlin *et al*., 2010) reported a significantly higher EQ-5D-3L utility index (0.92) among 66 OSA patients with a more severe form of OSA (average AHI 57 events/h, average ESS 12). These differences can be explained by the high prevalence of cardio-metabolic comorbidities (obesity, hypertension, type 2 diabetes) in our study population, but also by the fact that the 3 level EQ-5D form was used in the other report (Schmidlin *et al*., 2010).

Our baseline VAS was 63.71±17.74%, similar to the CPAP treated subgroup of d'Ambrosio et al. (59±19.8%) (D'Ambrosio *et al*., 1999), but significantly lower than other reports (80%) (Schmidlin *et al*., 2010). Comparable to other studies, we did not find a significant correlation between AHI and the two analyzed HR-QoL parameters (Dutt and Chaudhry, 2016).

The effect of CPAP on quality of life remains controversial (Dutt and Chaudhry, 2016; Jing *et al*., 2008; Schmidlin *et al*., 2010): while some reports have shown that CPAP use is able to "pseudonormalize" QoL up to the level of healthy controls, other analyses failed to show a significant QoL improvement after CPAP. These apparently antagonistic results arise due to different degrees of CPAP compliance among the studied populations. Lack of CPAP adherence is secondary not only

to the mask-associated discomfort, but also to a chronic lack of energy and motivation, which characterize most OSA patients (Chakravorty *et al*., 2002). Our study group showed borderline CPAP adherence, with an average CPAP use of 4 hours/night.

The increase in EQ-5D utility index observed in our study group is higher than previous reports (Chakravorty *et al*., 2002; Jenkinson *et al*., 1998). Another study also found a significant improvement after 3 months CPAP in both patient generated index (PGI) and 36-item Short Form Health Survey (SF-36) scores, but a relatively small change regarding EQ-5D-3L index (0.78 to 0.83) and EQ VAS (66.57% to 71.72%) (Jenkinson *et al*., 1997). While PGI was closely correlated with ESS (r=-0.49), the only non-significant correlation between the analyzed forms (PGI, SF-36, EQ and ESS) was that between PGI and the EQ index(Jenkinson *et al*., 1997). However, the previous study (Jenkinson *et al*., 1997) has important limitations, as it only included male patients and provided no information regarding apnea severity (average AHI) of their group.

Although the SF-36 is the most studied QoL instrument in OSA (Kuhn *et al*., 2017), the EQ-5D-5L VAS is also recommended for patients with sleep apnea(Schmidlin *et al*., 2010). An improvement in the EQ-5D-5L VAS similar to ours (11% versus 9.37%) was reported by a previous randomized control trial ($p<0.001$) (D'Ambrosio *et al*., 1999).

Since EQ-5D-5L does not take into consideration stamina and social life (which are severely impaired by chronic fatigue), some authors consider that the questionnaire may not be appropriate for OSA patients (Chakravorty *et al*., 2002; Jenkinson *et al*., 1997). Although this could explain why our analysis, as well as other studies (Chakravorty *et al*., 2002) did not find an association between AHI and the EuroQoL parameters, it does not account for the statistically significant improvement in both the EQ-5D-5L index and VAS after short term CPAP use.

CPAP has previously shown to be more effective in reducing cardiovascular risk and BP levels among symptomatic patients with higher ESS scores (Zhang, Luo, Qiao and Xiao, 2016). However, our results show that the impact on quality of life remains significant even in a group with an average ESS of 8,41, corresponding to a higher normal level of daytime sleepiness.

Although previous studies have shown an association between ESS and HR-QoL (Kuhn *et al*., 2017), we did not find a significant correlation between overall Epworth score, apnea severity and the analyzed EQ-5D-5L parameters. CPAP use was associated with a 4.44 point decrease in ESS score, similar to that reported by Patel et al. (Patel, White, Malhotra, Stanchina and Ayas, 2003) (4,75 points), but significantly lower than the one observed by a more recent study (Goel, Talwar and Jain, 2015) (8,5 points). These variations can be explained by the differences regarding OSA severity and CPAP adherence between groups, but also by the confounding influence of age, body mass index, smoking status and neuropsychiatric comorbidities (Antic *et al*., 2011).

Governmental policies regarding CPAP use (health coverage, device funding, revoking driving license in non-compliant OSA patients) significantly influence treatment compliance (Shapiro and Shapiro, 2010). OSA screening has recently become part of the compulsory medical examination to obtain or renew a driver's license in Romania, but only for group 2 license holders. The cost of CPAP is not covered by the public health care system and is relatively high, compared to the average income in Romania. Our results indicate that financial difficulties seem to play an important part in the decision to use CPAP in Romanian patients. However, our study group exhibited only borderline treatment adherence (4 hours/night) even while offered a free 2 months CPAP trial, suggesting that other factors (stigma, mask-related discomfort, pressure intolerance) also significantly influence CPAP compliance. As such, we would like to underline the need for medical education programs and OSA support groups, as well as the capital role of family encouragement in promoting CPAP adherence (Shapiro & Shapiro, 2010).

This is the first analysis of quality of life among Romanian OSA patients and also one of the first reports regarding EQ-5D-5L in the Romanian population. The most important limitations of our study are the lack of a control group and the presence of multiple cardio-vascular and metabolic comorbidities in our study population. However, the every-day OSA patient generally has a constellation of associated pathologies, thus underlining the clinical applicability of our results.

Conclusion

OSA has a significant impact on quality of life, according to the EQ-5D-5L questionnaire. Short-term CPAP use improves ESS and EQ-5D-5L results among OSA patients. Lack of CPAP adherence remains a major concern among Romanian patients with OSA. Income level influences the decision to continue CPAP use.

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