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UTILITY OF SCREENING QUESTIONNAIRES TO DETECT OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH OBESITY

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SUMMARY

Background: *Obesity is one of today's most concerning health problems due to increased cardiovascular risk, which is still the leading cause of death. Obstructive sleep apnea syndrome (OSAS) is certainly one of the important risk factors that links obesity and cardiovascular risk. There is a great need to evaluate obstructive sleep apnea (OSA) in obese patients. Today, there are easily available and applicable questionnaires (Epworth Sleepiness Scale (ESS), STOP, STOP-Bang (SBQ), Insomnia Severity Index (ISI) and Pittsburgh Sleep Quality Index (PSQI)) that could be very useful in clinical practice for this very purpose. The aim of this paper is to investigate the sensitivity and specificity of the questionnaires for OSA screening in obese patients with and without OSA.*

Patients and methods: *This cross-sectional study was carried out in the tertiary healthcare centre. The following questionnaires were used: ESS, STOP, SBQ, ISI, PSQI. 70 (58 female) adult patients with obesity (body mass index (BMI) > 30 kg/m2) were included.*

Results: *SBQ showed sensitivity of 75%, specificity of 75% at cut-off of 5.5 with the Youden index of 0.5, while PSQI had sensitivity of 78%, specificity of 67% at cut-off of 17.75 with slightly smaller Youden index 0.45. STOP and ESS had a sensitivity of 77% and 75%, respectively but with an even smaller Youden index (0.23 and 0.21), and ISI had the lowest sensitivity of 59% and the lowest Youden index (0.13) of the questionnaires we examined.*

Conclusion: *Our study results suggest that SBQ and PSQI are best screening tools in detecting OSA in patients with obesity. Further study of these questionnaires and possible modifications are certainly important for future research.*

Keywords: *obstructive sleep apnea, obesity, screening, questionnaires*

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INTRODUCTION

Obesity, defined as body mass index (BMI) ≥30kg/m^2 is associated with an increased risk of cardiovascular disease (CVD), CVD mortality, and overall mortality in the general population (Dwivedi et al, 2020). One of the links between obesity and CVD includes obstructive sleep apnea syndrome (OSAS). It is a complex disorder that due to complete or partial obstruction of the upper airways, leads to periods of apnea and intermittent hypoxia during sleep. Episodes of hypoxia lead to continuous activation of the sympathetic nervous system, causing the elevation of circulating catecholamines serum levels and increased arterial blood pressure (Jordan et al. 2014). Those changes increase the overall cardiovascular risk (Ciavarella et al. 2018). Therefore, early recognition of OSAS is highly important, given that timely intervention may prevent or mitigate cardiovascular disease (Yeghiazarians et al. 2021). Overnight polysomnography is the golden standard for the diagnosis of obstructive sleep apnea (OSA) in symptomatic patients or patients with increased risk (Kapur et al. 2017). A home sleep apnea test (HSAT) can be used in uncomplicated adult patients with a moderate or severe risk of OSA. In case of negative, inadequate, or technically inconclusive results overnight polysomnography should be performed (Kapur et al. 2017). The Apnea-Hypopnea Index (AHI) is expressed by the number of apnea/hypopnea events per hour and is used in evaluating the severity of OSA. Patients are categorized into three groups: mild, moderate, and

severe OSA (Ciavarella et al. 2018). To diagnose OSA, the AHI has to be greater than 5 when the clinical symptoms are present, or if the AHI is greater than 15 in asymptomatic patients (Bingol et al. 2016).The high cost of overnight polysomnography, the long duration of the procedure, and the requirement for highly specialized professionals result in its insufficient availability. To overcome these disadvantages, more widely available screening methods were required. Due to the high prevalence of sleep disorders in the population, specific screening questionnaires and clinical screening models have already been developed. The wide questionnaires used are Epworth Sleepiness Scale (ESS), STOP questionnaire (SQ), STOP-BANG questionnaire (SBQ), Pittsburgh Sleep Quality Index (PSQI), and Insomnia Severity Index (ISI) (Morin 1993, Bastien et al. 2001, Johns 1991, Johns 1992, Buysse et al. 1989, Chung et al. 2016). Epworth Sleepiness Scale (ESS) consists of eight questions that examine the likelihood of falling asleep during the day in various situations. It is a validated test that is widely used for assessing daytime sleepiness regardless of the underlying condition. Patients with OSA may experience daytime sleepiness due to inadequate overnight rest. Although good in evaluating daytime sleepiness it does not consider important predisposing factors for OSA, such as BMI, gender, or neck circumference (NC). (Boyes et al. 2017, Panchasara et al. 2017). The STOP-BANG questionnaire (SBQ) was developed by Chung et al. (2008) and has since been validated in many languages. SBQ is a valuable tool in preoperative assessment and screening for OSA, especially in surgical patients with moderate to severe OSA (Bingol et al. 2016). It is characterized by high sensitivity and low specificity (Öztürk et al. 2019). Unlike ESS, SBQ considers a few predisposing factors for OSA, such as BMI and gender (Panchasara et al. 2017). Among all anthropometric measures, neck circumference (NC) was found to be in better correlation with the severity of OSA than BMI. (Öztürk et al. 2019). Developed by Buysse et al. (1989), the Pittsburgh Sleep Quality Index (PSQI) is also one of the most used questionnaires for screening sleep-relateddistrubances. It is intended to reliably measure sleep quality in many sleep disorders and to discriminate between good and bad sleepers. It consists of 19 self-rated questions and 5 questions rated by the bed partner or a roomate (Buysee et al. 1989). The Insomnia Severity Index has seven items, ranging from 0 to 4 on the Lickert scale with the range of symptom severity from 0 (no symptom) to 4 (very severe). The first three items describe initial, middle, and late insomnia. The last four items refer to dissatisfaction with sleep, impairment of quality of life, worry, and the impairment of daily functioning due to sleep problems, respectively (Morin 1993, Bastien et al. 2001). Since OSA can manifest with a variety of symptoms such as excessive daytime sleepiness, sleep fragmentation and even parasomnia, that overlap with symptoms found in other sleep disorders, these questionnaires may be useful in distinguishing patients with OSA. Hence, the aim of this study is to investigate the sensitivity and specificity of these five questionnaires for screening OSA (ESS, SQ, SBQ, PSQI, and ISI) in obese patients with and without OSA.

SUBJECTS AND METHODS

This cross-sectional study was carried out at the Croatian Obesity Treatment Referral Centre of the Division of Endocrinology, University Hospital Centre Zagreb which is a collaborative center of the European Association for the Study of Obesity (EASO). The study was approved by the Ethics Committee of our institution (Permit class: 8.1-18/161-2, No. 02/21 AG). All of the participants signed an informed consent form. The following questionnaires were used: ESS, STOP, STOP-Bang (SBQ), Insomnia Severity Index (ISI) and Pittsburgh Sleep Quality Index (PSQI). All of the above questionnaires are already validated in the Croatian language. 70 (58 female and 12 male) participants were included. Included were adults ≥18 years of age, who were obese (defined as BMI>30 kg/m^2). Exclusion criteria were pregnancy, previous diagnosis and the treatment of OSA, recent airway cancer, airway surgery, or any airway obstruction, as well as decompensated cardiopulmonary disease. Overall, 70 participants underwent HSAT and completed the following questionnaires: ESS, STOP(4), SBQ, ISI and PSQI. HSAT was performed on the device Somnomedics 2020. Randersacker, Germany. Descriptive statistics, a series of Spearman's rank correlation coefficients, Welch t-tests, chi-squared tests, and linear and ordinal logistic regression analyzes were performed. Based on the previous, ROC curves were constructed and the sensitivity, specificity, and Youden index for each of the possible cut-offs on the questionnaires mentioned were calculated where the existence of OSA on polysomnography (AHI> 5) was used as the reference variable. Average scores on SBQ were calculated for men and women, patients with diabetes and without, pre-diabetes and without, with hypertension and without. Finally, we tested by F-test whether hypertension and diabetes explain a significant additional part of the variance of the criterion variable. Statistical analysis was performed in the R program (version 3.6.1) (R Core Team 2022).

RESULTS

The mean age was 50.29 ± 11.91 years. The average BMI was 44.64 ± 8.12 kg / m^2. 48 (38 female and 10

male) subjects had OSA (AHI index greater than 5). 31 patients had hypertension (23 of whom had OSA and 8 did not have). SBQ showed sensitivity of 75%, specificity of 75% at cut-off of 5.5 with the Youden index of 0.5, while PSQI had sensitivity of 78%, specificity of 67% at cut-off of 17.75 with slightly smaller Youden index 0.45. STOP (4 questions) and ESS had a sensitivity of 77% and 75% but with an even smaller Youden index (0.23 and 0.21), and ISI had the lowest sensitivity of 59% and the lowest Youden index (0.13) of the questionnaires we examined (Table 1.)

Since we obtained the results as decimal numbers, and the score on the questionnaire as such must contain the whole number diagnostic accuracy indicators were observed through the construction of ROC curves (Table 2.), thus calculating the sensitivity, specificity and Youden index for each of the possible cut-offs on the instruments mentioned. We have shown the sensitivity, specificity, Youden index, PPV, and NPV for the individual possible cut-oofs as integers around the obtained decimal cut-offs (Table 3.).The ESS thus has a sensitivity of 75% at cut-off 5, a specificity of 46% with a Youden index 0.21, PPV 0.75 and NPV 0.46. SBQ at cut-off 5 has a sensitivity of 75%, specificity of 75% with the Youden index 0.5, PPV 0.86 and NPV 0.6. ISI at cut-off 8 has a sensitivity of 59%, specificity of 54% with Youden index 0.13, PPV 0.76, NPV 0.35. STOP (4Q) at cut-off 1 has a sensitivity of 77%, specificity of 46% with Youden 0.23, PPV 0.77, NPV 0.46. PSQI already has a sensitivity of 78% at cut-off 16, specificity of 67% with Youden 0.45, PPV 0.94, NPV 0.33.

Table 1. Diagnostic accuracy indicators of ESS, ISI, SBQ, STOP (4), and PSQI.

Instrument	Sensitivity	Specificity	*Cut-off*	Youden index
Epworth Sleepiness Scale	0.75	0.46	5.5	0.21
Insomnia Severity Index	0.59	0.54	8.5	0.13
STOP- Bang questionnaire	0.75	0.75	5.5	0.5
STOP questionnaire	0.77	0.46	1.5	0.23
Pittsburgh Sleep Quality Index	0.78	0.67	17.75	0.45

Table 2. ROC curves for each questionnaire examined.

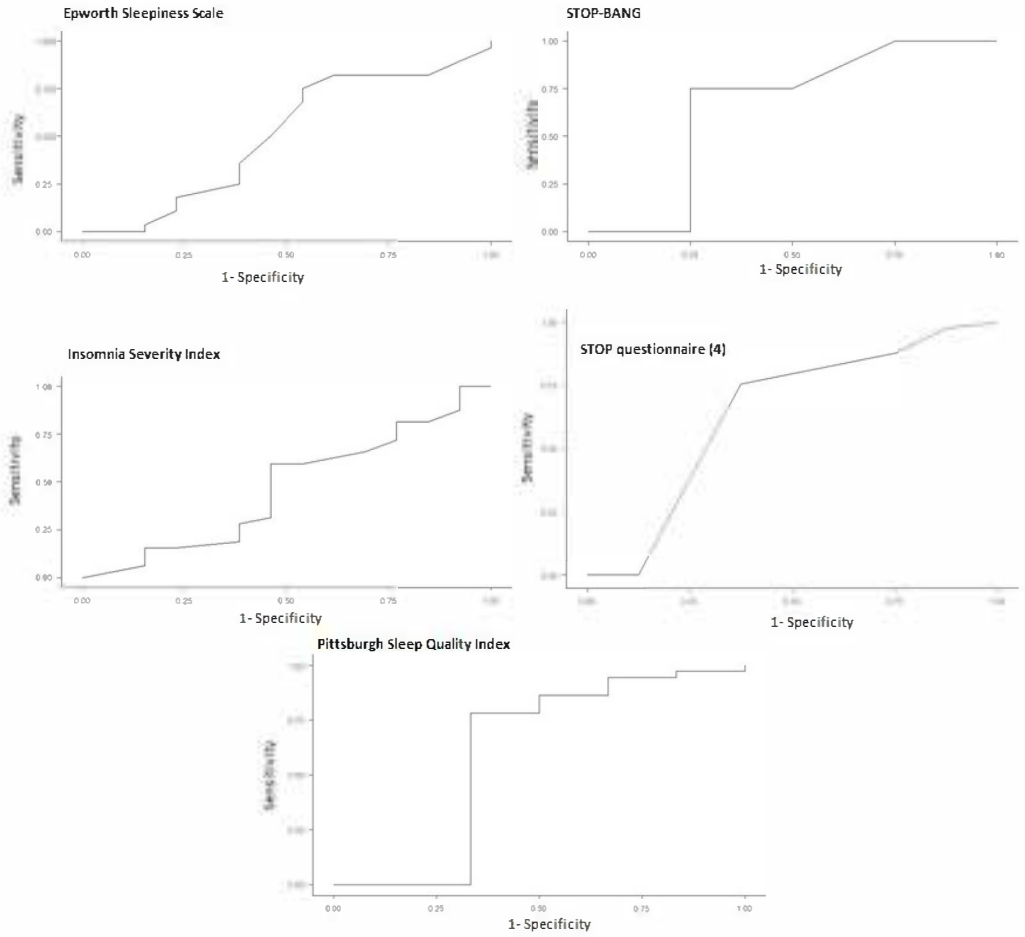

Table 3. Cut-offs, sensitivity, specificity, Youden index, PPV, NPV for the questionnaires studied.

Cut off	Sensitivity	Specificity	Youden	PPV	NPV
ESS					
4	0.82	0.38	0.2	0.74	0.5
5	0.75	0.46	0.21	0.75	0.46
6	0.68	0.46	0.14	0.73	0.4
7	0.5	0.54	0.04	0.7	0.33
8	0.36	0.62	-0.02	0.67	0.31
9	0.25	0.62	-0.13	0.58	0.28
10	0.18	0.77	-0.05	0.62	0.3
11	0.11	0.77	-0.12	0.5	0.29
12	0.04	0.85	-0.11	0.33	0.29
13	0	0.85	-0.15	0	0.28
14	0	0.92	-0.08	0	0.3
15	0	1	0	0	0.32
SBQ					
1	0	1	0	0	0.33
2	0	0.75	-0.25	0	0.27
3	0.12	0.75	-0.13	0.5	0.3
4	0.38	0.75	0.13	0.75	0.38
5	0.75	0.75	0.5	0.86	0.6
6	0.75	0.5	0.25	0.75	0.5
7	1	0.25	0.25	0.73	1
8	1	0	0	0.67	0
ISI					
7	0.59	0.46	0.05	0.73	0.32
8	0.59	0.54	0.13	0.76	0.35
9	0.56	0.54	0.1	0.75	0.33
10	0.53	0.54	0.07	0.74	0.32
11	0.53	0.44	0.54	0.7	0.28
12	0.41	0.54	-0.05	0.68	0.27
13	0.38	0.54	-0.08	0.67	0.26
14	0.31	0.54	-0.15	0.62	0.24
15	0.28	0.62	-0.1	0.64	0.26
STOP(4)					
1	0.77	0.46	0.23	0.77	0.46
2	0.27	0.77	0.04	0.73	0.31
3	0.07	0.92	-0.01	0.67	0.3
4	0	1	0	0	0.3
PSQI					
14	0	0.83	-0.17	0	0.12
15	0	0.67	-0.33	0	0.1
16	0.78	0.67	0.45	0.94	0.33
17	0.78	0.67	0.45	0.94	0.33
18	0.78	0.67	0.45	0.94	0.33
19	0.78	0.67	0.45	0.94	0.33
20	0.78	0.5	0.28	0.91	0.27

Table 4. Mean SBQ results depending on gender, diabetes, pre-diabetes and hypertension.

		SBQ result (mean)
Gender	Male	6.29
	Female	4.38
Diabetes	Yes	6.2
	No	4.57
Prediabetes	Yes	5.33
	No	4.63
Hypertension	Yes	6.17
	No	4

As all the results obtained were in favor of SBQ, average scores on SBQ were calculated for men and women, diabetics and non-diabetics, pre-diabetics and non-diabetics, and hypertensives and non-hypertensives (Table 4.).

Finally, we tested by F-test whether hypertension and diabetes explain a significant additional part of the variance of the criterion variable. Hypertension and diabetes explain a significant portion of the variance in response to SBQ above body mass index, with the individual contribution of hypertension being significant and diabetes not.

Table 5. Predictors according to criterion variables

Criterion variable	Model	Predictor	B	β	SD_B	*t*	p_t	*F*	df	p_F	R^2	F_Δ	df_Δ	$p_{F\Delta}$
AHI	BMI (only)	BMI	0.76	.31	0.36	2.13	.04*	4.54	1, 44	.04*	.09			
	BMI, hypertension and diabetes	BMI	0.7	.28	0.35	2.02	.0495*	3.23	3, 42	.03*	.19	2.43	2	.1
		Hypertension	8	.2	5.64	1.42	.16							
		Diabetes	11.3	.21	7.45	1.52	.14							
SBQ	BMI (only)	BMI (only)	0.09	.41	0.04	2.22	.04*	4.93	1, 24	.04*	.17			
	BMI, hypertension and diabetes	BMI	0.05	.26	0.03	1.61	.12	6.85	3, 22	.001**	.48	6.65	2	.006**
		Hypertension	2.06	.53	0.61	3.38	.003**							
		Diabetes	1.34	.27	0.78	1.71	.1							

Legend: B – non-standardized regression coefficient, β – standardized regression coefficient, SDB – standard deviation B, t – t-test value for testing the significance of a single predictor, pt – p-value of t, F – F-test value for testing of overall significance of the model, df – degrees of freedom F, pF – p-value F, R2 – coefficient of determination, FΔ – F-test value for comparison of two models, dfΔ – degrees of freedom for FΔ, pFΔ – p-value FΔ, * - p < .05, **-p<.01.

DISCUSSION

In the present sample, 68.5% of participants had OSA. Such proportion was markedly higher compared to prevalence estimates of 17% in men and 9% in women in the middle-aged employed population (Peppard et al. 2013), but in line with other studies in the obese population of similar age (Leong et al. 2013). According to our results, SBQ and PSQI have the best, both sensitivity and specificity for OSA screening in obese patients for preferred cut-off values (SBQ: cut-off 5.5; Youden index: 0.5 and PSQI: cut-off 17.75, Youden index: 0.45). ESS and STOP showed approximately the same quality with satisfactory sensitivity, and lower specificity for the corresponding cut-offs (ESS 5.5 and STOP 1.5) with the Youden index 0.21 and 0.23. ISI (Youden index 0.13) proved to be the weakest in OSA screening. To best of our knowledge, this is the first study that applied SBQ, SQ, PSQI, ESS and ISI in the population of obese individuals. Other studies have compared some of those scales, mostly in populations with sleep disturbances, including OSA. Our results comparing OSA screening tests are consistent with most research that also favours SBQ in OSA screening (Yeghiazarians et al. 2021). However, the results of the analysis of PSQI (sensitivity 78%, specificity 67% at cutoff 17.75 with Youden index 0.45) in OSA detection are surprising, since it is a questionnaire that measures sleep quality, rather than specific symptoms of OSA. Such a result is at odds with many other studies. For example, Nishiyama et al. (2014) conclude that PSQI should not be used for OSA screening because the score on PSQI depends more on psychological symptoms than polysomnography (10). On the contrary, in another Croatian study by Lusic Kalcina et al. (2017), PSQI was demonstrated to divide patients into good and poor sleepers (judging by total sleep time, REM duration, time spent awake during sleep and wakefulness after sleep onset (WASO) time), and this limit, according to their research, is at PSQI cutoff 9.5. The discrepancies across studies may arise from different study population i.e., screening instruments may differently perform in diverse groups. In the study of Nishiyama et al. (2014), the respondents were not obese, as reflected from their mean BMI of 25 or less, while in Lusic Kalcina et al. (2017), the subjects had BMI around 30. Of note, PSQI score positively correlated with the BMI (Ahmed Abdallah et al. 2021). In addition, female gender was also associated with global PSQI scores (Hung et al. 2013). Whereas the majority of our participants were predominantly women, in Nishiyama et al. the majority of participants were males. In agreement with our results, Kang et al. (2017) who evaluated subjective sleep quality using PSQI and obtained results that subjective sleep quality affects quality of life more than the objective indicator - the apnea-hypopnea index. Moreover, OSA individuals had decreased quality of life (Bjornsdottir et al. 2015), as did those with obesity (Sarwer et al. 2012), so the association between PSQI and OSA may be linked to the overall poor quality of life in our respondents with both OSA and obesity. However, we can only speculate that our participants with OSA had worse quality of life than those without OSA, because it was not analysed in the present study. According to our results, SBQ is better than ESS in OSA screening which is consistent with the work of Panchasara et al. (2017) which also gives an advantage to SBQ over ESS and conclude that ESS is not useful for OSA screening. On the other hand, they claim that SBQ is appropriate for OSA screening, but that the future could come up with a new, more specific questionnaire that would also include male, greater age and increased BMI. Unlike PSQI and ESS, SBQ is detecting typical OSA symptoms, such as snoring, tiredness, observed apnea and some of the risk factors for OSA. In agreement, the diagnostic performance of SBG of the SBQ was better than those of the ESS across all severities of OSA in a large sample of participants recruited in the Sleep Centre (Zheng et al. 2022). In general, ESS is considered a poor screening tool for OSA (Yeghiazarians et al. 2021). For example, excessive sleepiness was reported in 40% of individuals in whom OSA was not confirmed, 46% of patients with mild OSA, and 58% of those who were diagnosed with severe OSA

(Bjorvatn et al. 2015). Moreover, this scale measures only dozing behavior, and thus not distinguish the cause for the increased sleepiness, which could be induced by a number of other factors. Due to its negative impact of daily functioning, safety, productivity, and the risk of accidents (Lal et al. 2021), it nevertheless provides useful additional data during initial patient evaluation and follow-up visits. ISI was recognized as a good estimator of the severity of insomnia symptoms, but the score was not related to the presence / absence of OSA or the degree of OSA (Hagen et al. 2009), as our results show (sensitivity 59%, specificity 54% at cut-off 8.5 with Youden index 0.13). Other researches also confirm that the ISI cannot be used as an OSA screening test. However, insomnia often coexists with OSA (29.2% - 58.9%), and the ISI can be very useful in patients with suspected OSA in assessing cardiovascular and cerebrovascular risk, mood disorder propensity, and potential intolerance of CPAP devices (Hagen et al. 2009, Lam et al. 2017, Cho et al. 2018, Kim et al. 2017). The results of our sensitivity and specificity analysis for each individual SBQ cut-off contradict some other research. Other analyzes, however, not exclusively in obese patients, claim that the increase in SBQ cut-off leads to an increase in specificity, while the sensitivity is high at lower cut-offs (Kapur et al. 2017, Nagappa et al. 2015), while in our results the increase in cut-off increases sensitivity (from 12% at cut-off 3 to 75% at cut-off 5 with a constant specificity of 75% at cut-offs of 2-5). Numerous studies suggest the use of blood biomarkers in OSA screening. Fleming et al. (2018) demonstrated that the combination of HbA1c + CRP + EPO in a weighted formula with a cut-off of 9.95 had greater sensitivity (81%) and greater specificity (60%) than ESS (sensitivity 78%, specificity 19%) and STOP-Bang (sensitivity 75%, specificity 52 %). Future studies are needed to determine if the predictive value of using both SBQ and PSQI scales and the aforementioned biomarkers is higher in detecting patients with OSA, than each of the measures alone.

Limitations

Limitations of the present study include small sample size. Moreover, the pharmacological treatment was not recorded which may, in turn, induce daytime sleepiness or insomnia. Other potential factors which may influence sleep parameters were also not measured, such as caffeine, alcohol or nicotine consumption. Recent stressful life events may further disturb sleep pattern.

CONCLUSION

Finally, our results show that SBQ and PSQI are best screening tools in detecting OSA in patients with obesity. Since SBQ consists of 8 yes / no questions it turns out simpler, faster and more convenient. On the other hand, PSQI has 19 self-rated questions and 5 questions rated by the bad partner or roommate certainly provides a more precise, deeper insight that includes sleep quality. In the future, numerous new modifications of these questionnaires are possible, as well as the use of something completely new in OSA screening.

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Contribution of individual authors:
Filip Mustač, Martina Matovinović: study design, data collection, interpretation of data, literature searches, drafting the manuscript.
Tomislav Mutak: data collection, interpretation of data, drafting the manuscript
Barbara Barun, Marina Šagud, Darko Marčinko: interpretation of data, drafting and critically revising the manuscript.
All authors approved the final version.

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