The Clinical Predictors of Sleepiness Correlated with the Multiple Sleep Latency Test in an Asian Singapore Population

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Study Objectives: To explore the clinical predictors of sleepiness as objectively determined by the Multiple Sleep Latency Test with the Epworth Sleepiness Scale, age, body mass index, and overnight polysomnographic parameters at a tertiary referral center Sleep Disorders Unit.

Design: Retrospective, consecutive case series review.

Setting: A multidisciplinary sleep disorders unit in Singapore General Hospital, a tertiary-care university-affiliated hospital.

Patients: 72 consecutive patients evaluated for sleep disorders with overnight polysomnograms and Multiple Sleep Latency Tests between March 2002 and September 2002.

Interventions: N/A

Measurements and Results: Mean sleep latency on the Multiple Sleep Latency Test was 9.0 ± 4.4 minutes, and mean Epworth Sleepiness Scale score was 10.8 ± 5.8. On univariate analysis, mean sleep latency on the Multiple Sleep Latency Test showed a significant negative correlation with the Epworth Sleepiness Scale score, apnea-hypopnea index, body mass index, arousal index, and time spent below 90% oxygen saturation during overnight polysomnography. After performing multiple linear regression, only Epworth Sleepiness Scale score and apnea-hypopnea index remained significantly correlated (P = .039 and P = .008, respectively). An Epworth Sleepiness Scale score of 8 or above predicted a mean sleep latency on the Multiple Sleep Latency Test of less than 10 minutes with a sensitivity of 73.9% and specificity of 50.0%.

Conclusions: The Epworth Sleepiness Scale and apnea-hypopnea index are useful predictors of sleepiness in our Asian Singapore population.

Key Words: Epworth Sleepiness Scale, Multiple Sleep Latency Test, apnea-hypopnea index, polysomnogram

Citation: Leng PH; Low SY; Hsu A; Chong SF. The clinical predictors of sleepiness correlated with the Multiple Sleep Latency Test in an Asian Singapore population: predictors of sleepiness. *SLEEP* 2003;26(7):878-81.

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INTRODUCTION

SLEEPINESS IS A SUBJECTIVE COMPLAINT THAT IS OFTEN ENCOUNTERED IN THE SLEEP CLINIC. Over the years, sleepiness scales and diagnostic tests have been developed with the intention of assessing sleepiness in a more objective and standardized manner. This is crucial in the diagnosis of sleep disorders, in monitoring therapeutic efficacy, and for the standardization of research studies. More importantly, failure to recognize sleepiness is related to significant morbidity and mortality.[1]

Most of the published literature on the validity and reliability of measures of sleepiness have been performed in the Western population. At the Singapore General Hospital Sleep Disorders Unit, we see a spectrum of sleep disorders in a multiracial and multilingual population. The Singapore population consists of 76.7% Chinese, 13.9% Malay, 7.9% Indian, and 1.5% other races.[2] This diversity could make the interpretation of the complaint of sleepiness in our multiracial population difficult. Cultural influences and different racial attitudes toward sleepiness may also exist, further confounding the problem.

A study done in our institution previously showed that people who snore and had daytime sleepiness had a mean sleep latency on the Multiple Sleep Latency Test (MSLT) of less than 10 minutes.[3] Using the mean sleep latency on MSLT as our gold-standard objective test for sleepiness, we set out to investigate the following: (1) Is the Epworth Sleepiness Scale (ESS) able to reliably assess sleepiness in our population? (2) Is the arousal index correlated with sleepiness? and (3) Are there any other clinical and polysomnography (PSG) parameters (eg, age, body mass index [BMI], apnea-hypopnea index [AHI], sleep-onset time, or time spent below 90% oxygen saturation during overnight PSG) that are correlated with the MSLT measure of sleepiness?

Disclosure Statement
No significant financial interest/other relationship to disclose.

Submitted for publication January 2003
Accepted for publication May 2003
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METHODS

The Singapore General Hospital Sleep Disorders Unit is a multidisciplinary tertiary referral center for sleep disorders in Singapore.

Patient Selection

We retrospectively looked at 72 consecutive patients who presented to our Sleep Disorders Unit from March 2002 to September 2002. Our patient population was not confined to any specific diagnosis; hence, it was a reflection of the type of cases sleep physicians normally encounter at our Sleep Disorders Center. Patients were included only if they had both baseline PSG and MSLT performed. The MSLT studies were ordered based on individual physicians' clinical assessment, particularly if they had wanted to assess sleepiness objectively, rule in narcolepsy, or do both. All of these patients had completed a comprehensive questionnaire with regard to their sleep habits, underlying medical problems, and specific questions relating to the diagnoses of sleep-disordered breathing (SDB), periodic limb movement disorder (PLMD), narcolepsy, circadian rhythm disturbances, and substance abuse.

The ESS

The ESS is an 8-question self-administered questionnaire, which has been previously described.[4] A nurse practitioner was available for translation, if needed, because our population was not entirely English speaking.

The Baseline PSG

The overnight PSG was performed on the Compumedics E series system (Australia) with a 16-polygraph channel. The electroencephalogram electrodes were placed based on the international 10-20-20 system (C4/O1, C3/O2, O2/A1 and O1/A2). Airflow limitation was detected using a nasal pressure transducer. The oxygen saturation was measured using the standard pulse oximeter. The other channels on the PSG were set up in the usual standard manner.

The MSLT

The MSLT was performed according to established published standards and guidelines.[5] Sleep latency was defined as the time from lights out to the first epoch of sleep, and rapid eye movement (REM) latency as from the first epoch of sleep to the first epoch of REM.

A mean sleep latency on MSLT of less than 5 minutes is regarded as very sleepy, 5 minutes to less than 10 minutes as moderately sleepy, and 10 minutes or greater as normal.

Scoring

All studies were initially scored by the sleep technologists and later verified by 1 investigator who is a diplomate of the American Board of Sleep Medicine (LPH) and the 2 board-certified sleep technologists. Sleep stages were scored according to Rechtschaffen and Kales standard scoring criteria.[6] Arousals were scored in accordance to the American Sleep Disorders Association (ASDA) Task Force guidelines on the scoring of arousals.[7] The arousals were then classified into spontaneous (when no obvious cause of the arousal was found), related to SDB, or related to PLMD for further analysis.

Obstructive apneas were defined as the complete cessation of breathing for at least 10 seconds, accompanied by discernible thoracoabdominal effort. A central apnea was defined as the complete cessation of airflow in the absence of thoracoabdominal effort. Hypopneas were scored if there was a reduction in the airflow accompanied by at least a 3% desaturation or an arousal.[8] Periodic limb movements (PLM) were scored based on the guidelines as set forth by the ASDA document.[9]

An AHI of 5 to 15 events per hour was regarded as mild, 16 to 30 events per hour as moderate, and more than 30 events per hour as severe SDB. The central apnea index of more than 5 events per hour was considered significant. A PLM index of more than 5 events per hour was also considered significant.

After evaluating the clinical history, completed questionnaire, and PSG and MSLT results, a diagnosis or aggregate of diagnoses was made based on the International Classification of Sleep Disorders (ICSD) 2000 that may account for the cause of sleepiness in our patient population.

Statistical Analyses

All statistical analyses were performed using SPSS statistical software package version 10 (SPSS Inc, Chicago, Illinois). In order to assess the relationship between the mean sleep latency on MSLT with patient and PSG parameters, initial scatter plots were obtained that showed a continuous linear relationship between some variables and the mean sleep latency on MSLT. Hence Pearson product moment correlation was used, with a *P* value at the .01 level (2-tailed) being taken as statistically significant. A multiple linear regression analysis with stepwise variable selection method was subsequently performed on all the variables that showed a significant univariate association with the mean sleep latency on MSLT. In order to establish the sensitivity and specificity of the ESS scores and AHI in predicting a mean sleep latency of less than 10 minutes on the MSLT, receiver operating characteristic (ROC) curves for these 2 indexes were obtained.

RESULTS

The study population's characteristics and overnight PSG and MSLT results of all 72 patients are summarized in Table 1. The final diagnoses in all patients, based on ICSD 2000 coding, are shown in Table 2. Obstructive sleep apnea was present in 56.9% of this population.

Univariate analysis showed that there was a statistically significant negative linear correlation between ESS score and mean sleep latency on MSLT. This negative correlation was also seen with AHI, BMI, total

Table 1—Patient characteristics and polysomnographic and Multiple Sleep Latency Test results

Characteristic	Value
Age, y	41.9 ± 11.7
Male sex, no. (%)	47 (65.3%)
Race, no. (%)	
Chinese	60 (83.3%)
Malay	4 (5.6%)
Indian	7 (9.7%)
Other	1 (1.4%)
Mean body mass index, kg/m^2	26.2 ± 5.6
Mean Epworth Sleepiness Scale score	10.8 ± 5.8
Sleep-onset time on polysomnogram, min	
Median (range)	11.5 (0.5 – 136.5)
Total sleep time, min	
Median (range)	355.5 (199.5 – 467.5)
Time below SpO_2 90%, min	
Median (range)	1.2 (0 – 335.2)
Apnea-hypopnea index, events/h	
Median (range)	8.2 (0 – 96.7)
Arousal index, events/h total	
Median (range)	23.6 (5.7 – 104.5)
Sleep-disordered breathing	
Median (range)	4.2 (0 – 104.5)
Periodic limb movement disorder	
Median (range)	0 (0 – 16.4)
Spontaneous	
Median (range)	8.4 (0 – 34)
Mean sleep latency on MSLT, min	9.0 ± 4.4

MSLT refers to Multiple Sleep Latency Test; SpO_2, oxygen saturation

Table 2—Clinical diagnosis for all 72 patients

Diagnosis*	Patients, no.
OSA	41
PLMD	12
OSA + PLMD	7
Narcolepsy	4
Idiopathic hypersomnolence	2
OSA + central sleep apnea	2
Mood-related sleep disorder	2
Parasomnia	1
PLMD + chronic pain syndrome	1

*Diagnosis as defined by ICSD 2000.
OSA refers to obstructive sleep apnea; PLMD, periodic limb movement disorder

Table 3—Univariate analysis correlating variables with mean sleep latency on Multiple Sleep Latency Test

	Pearson correlation coefficient	P value
ESS	-0.361	.002 *
AHI	-0.406	.000 *
BMI	-0.355	.002 *
Arousal index		
Total	-0.355	.002 *
SDB	-0.405	.000 *
PLMD	-0.282	.016
Spontaneous	0.191	.108
Time below SpO_2 90%	-0.367	.002 *
PSG sleep onset	0.189	.111
Age	0.123	.301

*Correlation is significant at the .01 level (2-tailed).
MSLT refers to Multiple Sleep Latency Test; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index, BMI, body mass index; SDB, sleep-disordered breathing; PLMD, periodic limb movement disorder; SpO_2, oxygen saturation; PSG, polysomnogram.

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arousal index, arousal index secondary to SDB, and time spent below 90% oxygen saturation during overnight PSG. This was not seen with an arousal index secondary to PLMD, arousal index secondary to spontaneous arousals, sleep-onset time on PSG, or age (Table 3).

When these variables were further analyzed using a multiple linear regression with stepwise variable selection method, only the correlations between mean sleep latency on MSLT with ESS scores and AHI remained statistically significant ($P = .039$ and $P = .008$, respectively). The coefficient of determination R^2 for the regression of ESS score and AHI on MSLT was 0.215.

The ROC curves were plotted for both ESS scores and AHI using a mean sleep latency on MSLT of less than 10 minutes. The area under the curve for the ROC using the ESS score was 0.675 (95% CI, 0.546-0.804; $P = .014$), and that for the AHI was 0.580 (95% CI, 0.449-0.711; $P = .263$). However, when a mean sleep latency on MSLT of less than 5 minutes was used, the area under the curve increased to 0.774 for the ESS score (95%, CI 0.651-0.897; $P = .001$) and to 0.752 for AHI (95% CI, 0.593-0.912; $P = .002$).

We found that an ESS score of 8 or above predicted a mean sleep latency on MSLT of less than 10 minutes with a sensitivity of 73.9% and specificity of 50.0% (positive predictive value, 72.3%; negative predictive value, 52.0%).

DISCUSSION

The correlation of clinical predictors with sleepiness is indeed variable. The reasons for this observation are not entirely clear. Current methods to objectively quantify sleepiness may only capture some components of the sleepiness. Furthermore, we have not identified all the important variables that would allow a complete assessment of sleepiness. Perhaps we are not measuring sleepiness per se, but the *tendency* to sleepiness that is a consequence of a disturbed homeostatic sleep-wake process.[10] We also speculate that different pathophysiologic conditions may have a variable impact on the perception of sleepiness. This may result in one instrument being more reliable than another in predicting sleepiness in different clinical conditions.

Given the current limitations and a paucity of data regarding the assessment of sleepiness in our Asian population, we undertook this study and found that both the ESS score and AHI predicted sleepiness when correlated with mean sleep latency on MSLT. The other parameters of BMI, total arousal index, arousal index secondary to SDB, and time spent below 90% oxygen saturation during overnight PSG did not correlate with sleepiness following multiple linear regression analysis. Despite this association with sleepiness, the ESS score and AHI could explain only about 20% of the variance in the MSLT data ($R^2 = 0.215$). This would suggest that other predictors of sleepiness exist but were not identified in our study.

There are several limitations in this study. Firstly, we have not established in our own population the validity and reliability of the MSLT nor the mean sleep latency on MSLT that would help us define sleepiness. This is because we lacked an appropriate control group of nonsleepy people, and, hence, we have used the cutoff for mean sleep latency on MSLT that has been accepted in the literature. Secondly, our results may not be applicable to the general population due to a selection bias as a consequence of a retrospective study design. We tried to minimize this by studying consecutive patients who had both baseline PSG and MSLT performed. Of note, the racial composition of our sample population was similar to that of the general Singapore population. Furthermore, of the total number of 393 diagnostic PSGs performed during this study period, 321 patients had only PSGs. These 321 patients had a mean age of 45.6 ± 13.1 years, with 72.3% of them being men. Their racial composition consisted of 81% Chinese, 9% Malay, 7.5% Indian, and 2.5% other races. These demographics are similar to that of our study population, which comprised 18% of the total number of patients seen at our Sleep Disorders Unit over the 6-month study period. Thirdly, although we set out to investigate markers of sleepiness regardless of etiology, it is still possible that different underlying pathophysiologic states may yield different predictors of sleepiness. Similarly, different races may manifest different predictors of sleepiness, but we analyzed a heterogeneous Asian population together. This was because our study was not sufficiently large to perform subgroup analysis to investigate these possibilities, but further studies in this area would be interesting and valuable.

The data on the ESS as a predictor of sleepiness based on the current literature is conflicting. The ESS is dependent upon recall of perception or tendency to sleepiness in real-life situations, whereas the MSLT is performed in a laboratory setting in a protocol fashion. Murray has shown that the ESS is well validated and reliable as a tool for assessing sleepiness.[11,12] Subjects with a low mean sleep latency on the MSLT generally have an increased propensity to sleepiness as measured by the ESS, although the cutoff of ESS score for defining sleepiness may differ in different study populations. Chervin et al disputed this when they found that the correlation of ESS score and mean sleep latency on MSLT was poor in patients with OSA.[13] Benbadis et al also did not find a correlation between the ESS score and mean sleep latency on MSLT in a heterogeneous clinical population.[14] While the ESS is widely used in our Sleep Disorders Center, we were concerned about its reliability in assessing sleepiness, given the language differences and possible racial variability in the perception of sleepiness. In our study, we found that an ESS score of 8 or greater predicted a mean sleep latency on MSLT of less than 10 minutes with a sensitivity of 73.9% and a specificity of 50.0% (positive predictive value, 72.3%; negative predictive value, 52.0%). We deliberately chose a high sensitivity and high positive predictive value to determine a cutoff value for the ESS score because the consequences of missing a diagnosis of sleepiness can be costly. The ESS is only a modest predictor of sleepiness if the cutoff for mean sleep latency on MSLT is less than 10 minutes (area under ROC curve = 0.675, $P = .014$). However, there was a trend toward a stronger association in our study population when a lower cutoff for mean sleep latency on MSLT was used (a cutoff of less than 5 minutes produced an area under ROC curve of 0.774, $P = 0.001$).

The correlation of AHI with sleepiness in our study was borne out in both univariate and multivariate regression analyses. This finding is consistent with the study by Chervin and Aldrich[15] but others did not find this association to be significant.[13,16] In their large community-based study, Gottlieb et al reported that the ESS score correlated with AHI on the PSG.[17] Thus the value of AHI as a predictor of sleepiness is still yet to be fully defined.

One of our hypotheses was that the arousal index is correlated with sleepiness. This was not shown in our study. We were unable to demonstrate a relationship between sleepiness and the arousal index as scored using the ASDA criteria and sleepiness, which is consistent with results previously published.[18,19] However, 1 study reported that the arousal index did correlate with sleepiness, but the authors' scoring of arousals was different than ours,[20] while another found that the respiratory arousal index was strongly correlated with MSLT results.[21] Until the significance of electroencephalographic arousals is better clarified, one can only postulate the reasons for this observation. Boselli et al demonstrated that in a cohort of normal patients who did not have sleepiness, the arousal index increased with age.[22] This suggests that arousals may be an epiphenomenon in sleep, rather than a pathologic process, unless a threshold of arousal index is met. Furthermore, measurement of arousals is done on a few standard cortical reference leads, which may not be a complete representation of electroencephalographic arousals from sleep. While we cannot ignore the role of arousals in sleep fragmentation, more data are needed in establishing what the normal arousal index is in both the nonsleepy and sleepy populations.

In conclusion, the ESS score and AHI are modest predictors of sleepiness in our Asian Singapore population seen at a tertiary referral sleep disorders center. We have shown in this study that both these variables have significant correlation with sleepiness as measured by the mean sleep latency on MSLT. The study was not intended to test the clinical utility of the MSLT but, rather, to provide a reference point for managing patients with pathologic sleepiness in our Asian population using

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available clinical and PSG parameters that may predict sleepiness. Current clinical parameters that have been established to predict sleepiness are often interrelated and have varying correlations with objective measures of sleepiness. While we found the correlation of ESS score and AHI to be only a modest one, it is perhaps comforting to note that the perception of sleepiness, be it from a Western or Asian population, may not be so different after all.

ABBREVIATIONS

AHI: apnea-hypopnea index
ASDA: American Sleep Disorders Association
BMI: body mass index
ESS: Epworth Sleepiness Scale
ICSD: International Classification of Sleep Disorders
MSLT: Multiple Sleep Latency Test
OSA: obstructive sleep apnea
PLMD: periodic limb movement disorder
PSG: polysomnogram
REM: rapid eye movement
ROC: Receiver Operating Characteristic
SpO_2: oxygen saturation on pulse oximetry
SDB: sleep-disordered breathing

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