

Project title:

**Sleep Deprivation, Circadian Disruption and Mild
Cognitive Impairment among Patients with Silicosis
in Hong Kong**

Final Report

(31 March, 2021)

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The work described in this report was substantially supported by a grant from Pneumoconiosis Compensation Fund Board of the Hong Kong Special Administrative Region, China.

Executive summary

Objectives:

Recent research in general population showed that sleep deprivation and decreased amplitude of circadian rhythm increased the risk of dementia/mild cognitive impairment (MCI). However, it remains uncertain if population-based research can be directly generalized to the pneumoconiosis patients who have less healthy lungs than the general population. Therefore, the main objectives of this project are to investigate the prevalence of MCI and sleep deprivation among patients with pneumoconiosis in Hong Kong, and further to examine the influence of sleep deprivation and weakened circadian rhythm on the prevalence of MCI.

Methods:

This was a cross-sectional study including two parts. Part I study was a questionnaire-based survey comprising of 747 pneumoconiosis patients and 233 community participants who were recruited between October 2018 and September 2020.

Cognitive function was assessed by the Hong Kong version of Montreal Cognitive Assessment (HK-MoCA) and the Cantonese version of Mini-Mental State Examination (CMMSE). Subjective sleep pattern was examined by the Pittsburgh Sleep Quality Index (PSQI). Sociodemographic, medical and behavioral information were also collected. Part II was an actigraphy assessment sub-study containing 191 pneumoconiosis patients and 211 community subjects. All participants in Part II study were invited to continuously wear the actigraphy for 120-168 hours to measure circadian rhythms represented by 4 main parameters including percent rhythm,

amplitude, the midline estimation of statistic of rhythm (mesor) and acrophase. Generalized linear models and multivariate logistic regression were performed to examine the relationships of sleep quality and circadian activity rhythm with cognitive function and prevalence of MCI.

Results:

Compared with the community subjects, patients with pneumoconiosis had lower scores of both HK-MoCA (19.6 vs. 21.9, $p<0.001$) and CMMSE (25.2 vs. 26.2, $p<0.001$), and higher prevalence of MCI or cognitive impairment detected by either HK-MoCA test (18.5 %, 138 cases vs. 12.6 %, 29 cases, $p=0.038$) or CMMSE (54.8%, 403 cases vs. 38.3%, 88 cases, $p<0.001$). Although the significant differences in the global scores tended to diminish after adjustment of confounders, pneumoconiosis patients still had significantly lower scores than the community referents in specific components “naming” (-0.13 units), “language” (-0.12 units), “abstraction” (-0.32 units) and “delayed recall” (-0.32 units) in the HK-MoCA test, as well as the CMMSE’s component “orientation” (-0.30 units).

A significantly higher PSQI global score (8.0 vs. 6.5, $p<0.001$) and a higher proportion of poor sleepers defined as a global PSQI score > 5 (67.7% vs. 51.9%, $p<0.001$) were observed in pneumoconiosis patients than those of the community subjects. After controlling for potential confounders, pneumoconiosis patients who had higher global PSQI scores or the scores of specific component “sleep latency”, “habitual sleep efficiency” and “sleep disturbances” were negatively associated with HK-MoCA score. Patients with sleep disturbances was positively associated with increased risk of MCI or cognitive impairment (adjusted OR=1.48, 95%CI: 1.03, 2.12). In addition, sleep duration > 9 h/night or <5 h/night was significantly associated

with an increased risk of MCI and a lower score of HM-MoCA, showing a U-shaped curve. A similar pattern of association was also observed for CMMSE.

Dampened circadian rhythm was observed among pneumoconiosis patients compared with the community subjects, showing a significantly decreased median of mesor (241.1 vs. 268.3, $p=0.012$) and advanced median of acrophase (1:30PM vs. 2:06PM, $p=0.038$). Results from multivariate regression model further demonstrated that pneumoconiosis patients were more likely to have a low mesor value than that of the community referents (Adjusted OR=2.06, 95% CI: 1.20, 3.55).

In pneumoconiosis patients, multivariate models revealed significantly positive associations between amplitude and MCI detected by HK-MoCA (adjusted OR=3.35, 95%CI: 1.03, 10.9) and CMMSE (adjusted OR=2.07, 95%CI: 0.96, 4.51), as well as between high mesor and low HK-MoCA total score (β coefficient, -1.38, $p<0.05$) or CMMSE total score (β coefficient, -0.96, $p<0.10$). Using the community referents with higher mesor as reference, multivariate models showed that patients with lower mesor (adjusted OR=1.97, 95% CI: 1.00-3.85) had the highest prevalence of CMMSE-detected MCI or cognitive impairment. Results were similar to those using the HK-MoCA tests, despite there was lacking of a significant association.

Among 94 pneumoconiosis patients with lung function data, compared with those with better lung function, pneumoconiosis patients with poorer lung function had lower HK-MoCA global scores (PEF: 20.0 vs. 21.7, $p=0.020$) and higher prevalence of MCI or cognitive impairment detected by CMMSE (FVC: 56 % vs. 32 %, $p=0.022$; or PEF: 54 % vs 33 %, $p=0.035$).

Conclusions

Our results demonstrated that pneumoconiosis patients have lower cognitive scores and higher prevalence of MCI or cognitive impairment than that of the community subjects; also, pneumoconiosis patients suffered from a higher proportion of poor sleep and weakened circadian activity rhythm. Poor sleep and weakened circadian activity rhythm patterns were associated with poor cognitive function in pneumoconiosis patients, and there was a U-shaped association between nocturnal sleep duration and MCI or cognitive impairment. We recommend health promotion programmes should be launched to mitigate cognitive decline and burden from cognitive impairment in workers with pneumoconiosis through improving sleep quality and optimizing sleep duration and circadian rhythm. However, it should be cautious that the associations obtained from this cross-sectional study need to be confirmed by a subsequent prospective cohort study, while the intervention strategies should be further consolidated in future randomized controlled trials.

Key words: pneumoconiosis, sleep, circadian rhythm, cognitive impairment.