The Factors Associated with Mild Cognitive Impairment (MCI) in Surgical Menopause Women

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Background and Objective: *As a sizeable proportion of persons with mild cognitive impairment will progress to frank dementia, early detection is an important strategy to prevent and decelerate the progression of cognitive decline. In Thailand, the prevalence of mild cognitive impairment in surgical menopause women has not been well established. The objectives of the present study were to determine the percentage and factors associated with mild cognitive impairment in women with surgical menopause.*

Material and Method: *Between October 2013 and July 2014, 200 eligible women at King Chulalongkorn Memorial Hospital were enrolled. The self-reported questionnaires were used to obtain the demographic data and the Thai version of the Montreal Cognitive Assessment (MoCA) was used to detect mild cognitive impairment (MCI). The MCI was diagnosed when the MoCA score was less than 25. The data were statistically analyzed using SPSS version 17 for student t-test, Chi-square test, and multiple regression analysis.*

Results: *The percentage of MCI in the present study was 43.5%. The univariate analysis showed that factors significantly related to MCI were marital status, educational levels, occupation, monthly income, and duration of hormone replacement therapy (HRT). Nevertheless, multiple regression analysis revealed that only older age at enrollment, marital status, low educational level, and low monthly income were significantly related to MCI.*

Conclusion: *Almost half of the surgical menopause women in the present study had MCI. Older age at enrollment, marital status, low educational level, and low monthly income were significantly related to MCI. Age at surgical menopause and HRT were not found to be associated with MCI in this study.*

Keywords: *Mild cognitive impairment (MCI), Surgical menopause*

With increasing life expectancy of global population due to continuing improvement of health care, various aging-related illnesses are more prevalence. Memory impairments are common consequence of the ageing process and are major public health concern. Recently, a special condition, named as mild cognitive impairment (MCI) was thought to be a transition phase between healthy cognitive ageing and dementia[1]. MCI refers to a clinical condition which persons experience memory loss to a greater extent than one would expect for age, yet they do not meet the criteria for Alzheimer's disease (AD)[2]. Many criteria were used to describe cognitive impairment. However, the inference is that patients with MCI already have brain pathology associated with dementia[3]. As a high prevalence of cognitive complaints frequently found during the menopause transition or early post menopause, the gonadal hormones may play an important role in the process[4,5].

Surgical menopause, on contrary to natural menopause, is a process which patients underwent an abrupt decrease not only estradiol but also other ovarian hormone production. In some previous studies, they found that early age at menopause was associated with faster decline in global cognition and hormone replacement therapy (HRT) within the window of opportunity period may delay the process of cognitive decline in surgical menopause patients[3,6,7]. However, the association of surgical menopause, HRT and MCI is not yet well established.

With the advent of the Montreal Cognitive Assessment (MoCA), which was well developed as a screening instrument to detect MCI, we were interested to assess the association of surgical menopause and

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MCI in our population with different demographic and genetic background with population in the other studies. The MoCA assesses multiple cognitive domains including attention, concentration, executive functions, memory, language, visuospatial skills, abstraction, calculation, and orientation. It has been widely used and translated to 36 languages and dialects[8]. In Thailand, Tangwongchai et al[9], reported a high correlation of MoCA Thai version (MoCA-T) and Thai-Mental Stage Examination (TMSE). MoCA-T is considered to be a simple and reliable screening instrument in clinical practice[9-11].

A sizeable proportion of patients with MCI will eventually progress to frank dementia. It is a silent public health concern. Therefore, early detection is an important strategy to prevent and decelerate the progression of cognitive decline. In Thailand, the burden of this condition and its consequences remain obscure. The prevalence of MCI in Thai surgical menopause women has not been well established. The objective of our study is to determine the percentage of MCI in surgical menopause women and to determine factors that would be associated with the condition.

Material and Method

This cross-sectional descriptive study enrolled 200 surgical menopause women who visited the Gynecologic and Menopausal clinics, King Chulalongkorn Memorial Hospital between October 2013 and July 2014. All participants signed informed consents after being thoroughly informed of the study protocol. The inclusion criteria were women whom underwent bilateral removal of ovaries ≥1 year prior to the commencement of the study and the surgical histology was benign. The exclusion criteria were women with histories of cerebrovascular diseases, psychosis, cancer, major head trauma, chemotherapy, radiotherapy, or those who were illiterate. The present study was approved by the Institutional Ethics Committee on September 24, 2013 and was supported by the Ratchadapiseksompotch Fund, Faculty of Medicine, Chulalongkorn University.

Demographic data and bio-psycho-social information were obtained from self-reported questionnaire. The information included age, marital status, year since menopause, educational level, occupation, income, medical and surgical history, history of HRT, exercise, sleeping disorder, family history of dementia, and self-awareness of forgetfulness.

Montreal Cognitive Assessment Thai version (MoCA-T), developed as a screening instrument to detected MCI, was used in the present study. The test is designed to assesses multiple cognitive domains i.e., attention, concentration, executive functions, memory, language, visuospatial skills, abstraction, calculation, and orientation. Sensitivity for MCI detection was on average 86% (range 77-96%). Sensitivity to detect AD was on average 97% (range 88-100%). The average specificity for MCI was 88%[8].

The MoCA-T used in the present study was reported to have high correlation with the TMSE. The sensitivity and specificity of MoCA-T were 0.8. Since it has been reported that the year of education were significantly associated with the score of MoCA-T. The compensation by adding 1 point for subjects with year of education less than 6 years was considered to be appropriate in Thai subjects[9-11]. Those with score below 25 were categorized as MCI.

The sample size of 200 participants were calculated from the prevalence from a previous study ($p = 0.13$, $d = 0.05$)[12]. Statistical analysis was done using SPSS version 17.0. Demographic characteristics were described using means and standard deviations (SDs) for continuous data. Frequency and proportions were used for categorical data. To compare the correlation between MCI and each factor we used t-test and X^2 test. We performed logistic regression analysis for duration of HRT, age at enrollment, marital status, educational level, occupation, and monthly income.

$$n = \frac{Z_{\alpha/2}^2 \, pq}{d^2}$$

$p =$ expected proportion e.g. prevalence

$p + q = 1$

$d =$ margin of error in estimating p

Results

Two hundred female participants were included, the mean age was 56.05 years (SD = 7.165 years). The mean age at surgical menopause was 45.53 years (SD = 5.727 years). Nearly half of the participants were menopause for more than 10 years. Approximately 51% of the participants had postmenopausal symptoms such as hot flashes, genitourinary symptoms, or insomnia, etc. Seventy percent of the participants used either estrogen or combined estrogen and progestogen therapy. Most of them had regular exercise and slept more than five hours a day. Surprisingly, nearly 60% of the participants' family members had dementia. Most of the participants felt that sometimes they experienced forgetfulness.

The percentage of mild cognitive impairment in the present study was 43.5%. They were classified

Table 1. Demographic characteristics and bio-psycho-social factors of subjects (200 women)

Characteristics	Number (%)
Age (years) (mean ± SD)	56.05±7.165
Age at menopause (years) (mean± SD)	45.53±5.727
Year since menopause	
1-5	61 (30.5)
6-10	42 (20.0)
>10	97 (48.5)
Marital status	
Married	122 (61.0)
Others (single, divorce, widow)	78 (39.0)
Educational level	
Primary school	52 (26.0)
Secondary and vocational school	48 (24.0)
Bachelor degree or higher	100 (50.0)
Occupation	
Government	67 (33.5)
Others (e.g. business)	102 (51.0)
Unemployed	31 (15.5)
Monthly income (Baht)	
≤10,000 (≤312 US$*)	39 (20.4)
10,001-20,000 (312-625 US$*)	54 (28.3)
20,001-50,000 (625-1,562 US$*)	66 (34.0)
>50,000 (>1,562 US$*)	33 (17.3)
Surgical period with menopause	
Oophorectomy after menopause	15 (7.5)
Oophorectomy before menopause	185 (92.5)
Postmenopausal symptoms	
No symptom	99 (49.5)
Hot flashes	63 (31.5)
Others	38 (19.0)
Hormone replacement therapy	
No HRT	53 (26.5)
Estrogen alone	124 (62.0)
Combined EP and tibolone	17 (8.5)
Duration of HRT	
0-5 years	135 (71.1)
6-10 years	31 (16.3)
>10 years	24 (12.6)
Exercise	
At least once a week	123 (61.5)
Less than once a week	18 (9.0)
Never	59 (29.5)
Sleep	
<5 hours	21 (10.5)
≥5 hours	179 (89.5)
Family history of dementia	
Yes	117 (58.5)
No	83 (41.5)

SD = standard deviation; HRT = hormone replacement therapy; combined EP = combined estrogen + progestin
* Considering 1 US$ = 32 Thai Bahts

by the MoCA score below 25. A univariate analysis was performed. Factors that significantly related to MCI were marital status, educational levels, occupation, monthly income, and duration of HRT (Table 2).

The multiple regression analysis revealed that older age at enrollment, marital status, low educational level, and low monthly income were significantly related to MCI (Table 3). There were no statistically significant associations among age at menopause, duration of menopause, history of HRT, underlying disease, exercise, duration of sleeping, family history of dementia, and personal awareness of forgetfulness in this study.

Discussion

The percentage of MCI in the studied population (mean age 56.05 years, mean age at surgical menopause 45.53 years, nearly half of the participants were menopause >10 years) was 43.5%. This is in contrast to the study of Lanchasak et al who found that the prevalence of MCI in natural menopause women was 13%[12]. Although it may be inappropriate to compare between two different studies due to the differences in population and screening tools for MCI, the three folds higher MCI in surgical menopause women when compared to those of the natural menopause was striking. This raises an interest of any association of acute loss of estrogen with MCI.

The initial univariate analysis showed that factors that were significantly related to MCI were marital status, educational levels, occupation, monthly income, and duration of HRT. Nevertheless, in multiple regression analysis, only older age at enrollment, marriage, low educational level, and low monthly income were found to be significantly associated with MCI. These findings were inconsistent with some previous studies[9,13,14]. However, the author found no correlation between age at surgical menopause or duration of HRT with MCI. This is in contrast to the analysis of two longitudinal cohort studies by Bove et al[3] showed that early age at surgical menopause was associated with faster decline in global cognition and increased Alzheimer's disease neuropathology. Their coefficients further indicated that the effect of each year of earlier surgical menopause on the rate of cognitive decline was equivalent to the effect associated with six months of aging.

The discrepancy of the results may be due to the different tools and outcome measure for the measurement of cognitive function. In our study, we used the MoCA-T to detect MCI, which is thought to

Table 2. Factors related to mild cognitive impairment (MCI) (univariate analysis)

Characteristics	MCI (n = 87)	Normal (n = 113)	p-value
Age (mean ± SD)	57.12±7.48	55.22±6.82	0.062
Age at menopause (mean ± SD)	45.59±5.99	45.47±5.54	0.884
Year since menopause (mean ± SD)	11.52±7.29	9.74±6.70	0.074
Marital status, n (%)			0.02
Married	61 (70.0)	61 (54.0)	
Others (single, divorce)	26 (30.0)	52 (46.0)	
Educational level, n (%)			<0.001
Primary school	42 (48.3)	10 (8.8)	
Secondary and vocational school	25 (28.7)	23 (20.4)	
Bachelor degree or higher	20 (23.0)	80 (70.8)	
Occupation, n (%)			<0.001
Government	15 (17.2)	52 (46.0)	
Business and others	54 (62.1)	48 (42.5)	
Unemployed	18 (20.7)	13 (11.5)	
Income (Bahts), n (%)			<0.001
<20,000 (<625 US$*)	44 (54.3)	25 (22.5)	
≥20,000 (≥625 US$*)	37 (45.2)	86 (77.5)	
Surgical period with menopause, n (%)			0.172
Before menopause	83 (95.4)	102 (90.3)	
After menopause	4 (4.6)	11 (9.7)	
Hormonal therapy, n (%)			0.323
Never use	20 (23.0)	33 (29.2)	
Ever use and current use	67 (77.0)	80 (70.8)	
HRT, n (%)			0.640
No HRT	21 (25.3)	32 (28.8)	
Estrogen alone	56 (67.5)	68 (61.3)	
Combined EP and tibolone	6 (7.2)	11 (9.9)	
Duration HRT, n (%)			0.029
0-5 years	24 (43.6)	52 (68.4)	
6-10 years	18 (32.7)	13 (17.1)	
>10 years	13 (23.7)	11 (14.5)	
Family history of dementia, n (%)			0.970
Yes	50 (58.1)	66 (48.4)	
No	36 (41.9)	47 (41.6)	
Forgetfulness, n (%)			0.946
Never	9 (10.5)	12 (10.6)	
Sometimes	69 (80.2)	92 (81.4)	
Always	8 (9.3)	9 (8.0)	
Duration of sleep, n (%)			0.950
<5	9 (10.3)	12 (10.6)	
≥5	78 (89.7)	101 (89.4)	

SD = standard deviation; HRT = hormone replacement therapy; combined EP = combined estrogen + progestin
* Considering 1 US$ = 32 Bahts

be a transition phase to dementia. This was in contrast to the other study that used Mini-Mental Stage Examination for measures of cognitive function. In addition, the population in our study were younger at enrollment (mean age 56.05 years vs. 78 years) of which we recruited only those with surgical menopause whilst Bove's cohort were older and included women having natural and surgical menopause.

Table 3. Multiple regression analysis

Characteristics	*p*-value	Adjusted odds ratio	95% CI for Exp (B)	
			Upper	Lower
Age#	0.006	1.072	1.020	1.127
Married	0.011	2.734	1.262	5.921
Primary school	<0.001	13.319	5.034	35.238
Monthly income <20,000 Thai Bahts (<625 US$*)	0.006	2.889	1.352	6.175

Older age at enrollment
* Considering 1 US$ = 32 Thai Bahts

The multiple regression analysis in our study did not show a significant association of HRT and MCI. This was not in accordance with Bove's study, which found that HRT use for at least 10 years, when administered within a 5-year perimenopausal window, was associated with decreased decline in global cognition. Apart from the differences in outcome measure and studied population stated earlier, 70% of our population who underwent oophorectomy received HRT while 53% of Bove's study population used HRT. Only 12.6% of our population used HRT more than 10 years, which was in contrast to Bove's study of which the mean duration of HRT was more than 13 years.

Nevertheless, there are some limitations of the present study due to being done in single institute, hospital-based nature. Although MoCA is a reliable screening instrument to detected MCI in clinical practice, another six-month follow-up test is needed for definitive diagnosis. Therefore, larger scale studies with a sensitive tool for the screening of MCI may be needed to confirm the association of surgical menopause and MCI. These studies are also needed to confirm the benefit of hormone replacement therapy in prevention or slow down the decline of global cognition and/or MCI particularly when it is given in the window of opportunity.

Conclusion

The present study revealed a high percentage of MCI (43.5%) in a group of hospital based surgical menopause women. Older age at enrollment, marriage, low educational level, and low monthly income were found to be significantly associated with MCI. Age at surgical menopause and HRT were not significantly associated with MCI in this study.

What is already known on this topic?

There have been high complaints of forgetfulness during menopause. HRT once believed to prevent and treat cognitive decline after menopause. Nevertheless, with the report of the adverse effects of HRT on cognitive function of the Women's Health Initiative (WHI) study, the role of HRT on cognitive function has been argued. However, recent studies[3,6,7] found that HRT use for at least 10 years, when administered within a 5-year perimenopausal window, was associated with decreased decline in global cognition, which in turn may be beneficial for these patients.

What this study adds?

MCI is a special condition that is thought to be a transition phase prior to dementia. Recently, a new tool i.e., MoCA was developed as a test with high sensitivity and specificity to detect MCI. Previous studies used various cognitive function tests that focused mostly on memory. Nevertheless, our study chose to use this new and sensitive cognitive function test (MoCA test) to test various domains of cognition in order to detect MCI. Unexpectedly, we found a high percentage of surgical menopause patients with mild cognitive impairment and it turned out that age at surgical menopause and hormone replacement therapy were not associated with MCI as general belief. This is probably due to the common complaints of memory loss during menopause. However, with the high percentage of MCI in this group of surgical menopause women, further studies are needed to look for any preventable or treatable factors in order to stop or slow down the occurrence of MCI in this particular group of women. Therefore, this may help lower the incidence of dementia particularly in surgical menopause women.

References
1. DeCarli C. Mild cognitive impairment: prevalence, prognosis, aetiology, and treatment. Lancet Neurol 2003; 2: 15-21.
2. Petersen RC, Doody R, Kurz A, Mohs RC, Morris JC, Rabins PV, et al. Current concepts in mild cognitive impairment. Arch Neurol 2001; 58: 1985-92.
3. Bove R, Secor E, Chibnik LB, Barnes LL, Schneider JA, Bennett DA, et al. Age at surgical menopause influences cognitive decline and Alzheimer pathology in older women. Neurology 2014; 82: 222-9.
4. Henderson VW. Cognitive symptoms and disorders in the midlife woman. Menopause Matters 2011; 36: 1-5.
5. Greendale GA, Wight RG, Huang MH, Avis N, Gold EB, Joffe H, et al. Menopause-associated symptoms and cognitive performance: results from the study of women's health across the nation. Am J Epidemiol 2010; 171: 1214-24.
6. Maki PM, Sundermann E. Hormone therapy and cognitive function. Hum Reprod Update 2009; 15: 667-81.
7. Maki PM, Henderson VW. Hormone therapy, dementia, and cognition: the Women's Health Initiative 10 years on. Climacteric 2012; 15: 256-62.
8. Julayanont P, Phillips N, Chertkow H, Nasreddine ZS. The Montreal Cognitive Assessment (MoCA): concept and clinical review. In: Larne AJ, editor. Cognitive screening instruments: a practical approach. London: Springer-Verlag; 2012: 111-52.
9. Tangwongchai S, Charernboon T, Phanasathit M, Akkayagorn L, Hemrungrojn S, Phanthumchinda K, et al. The validity of Thai version of The Montreal Cognitive Assessment (MoCA-T). Dement Neuropsychol 2009; 3: 172-6.
10. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999; 56: 303-8.
11. Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005; 53: 695-9.
12. Akkayagorn L. Tangwongchai S, Worakul P. Cognitive profiles, hormonal replacement therapy and related factors in Thai menopausal women. Asian Biomedicine 2009; 3: 439-44.
13. Deetong T, Puapornpong P, Pumipichet S, Benyakorn S, Kitporntheranunt M, Kongsomboon K. Prevalence and risk factors of mild cognitive impairment in menopausal women at HRH princess Maha Chakri Sirindhorn medical center. Thai J Obstet Gynaecol 2013; 21: 110-6.
14. Plassman BL, Langa KM, Fisher GG, Heeringa SG, Weir DR, Ofstedal MB, et al. Prevalence of cognitive impairment without dementia in the United States. Ann Intern Med 2008; 148: 427-34.
15. Nasreddine ZS. The Montreal Cognitive Assessment [Internet]. 2013 [cited 2013 Nov 30]. Available from: http://www.mocatest.org/

ปัจจัยที่สัมพันธ์กับภาวะพุทธิปัญญาเสื่อมระยะแรกในสตรีวัยหมดระดูจากการผ่าตัดรังไข่ทั้งสองข้าง

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ภูมิหลังและวัตถุประสงค์: ผู้ที่มีภาวะพุทธิปัญญาเสื่อมระยะแรกจำนวนหนึ่งได้เปลี่ยนแปลงไปเป็นภาวะสมองเสื่อม ดังนั้นการตรวจพบตั้งแต่ระยะเริ่มต้นจึงเป็นแนวทางที่สำคัญในการหาทางป้องกันและชะลอการถดถอยของภาวะพุทธิปัญญา ในประเทศไทยยังไม่มีข้อมูลเกี่ยวกับภาวะพุทธิปัญญาเสื่อมระยะแรกในสตรีที่หมดระดูจากการผ่าตัดรังไข่ทั้งสองข้าง การศึกษานี้มีวัตถุประสงค์ที่จะหาปัจจัยที่มีความสัมพันธ์กับภาวะพุทธิปัญญาเสื่อมระยะแรกในสตรีกลุ่มดังกล่าว

วัสดุและวิธีการ: สตรีวัยหมดระดูจากการผ่าตัดรังไข่ทั้งสองข้างที่มารับบริการ ณ คลินิกนรีเวชกรรม และคลินิกวิจัยสตรีวัยหมดระดู โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย ระหว่าง เดือนตุลาคม พ.ศ. 2556 ถึง กรกฎาคม พ.ศ. 2557 จำนวน 200 คน ที่มีคุณสมบัติตามเกณฑ์การศึกษาจะได้รับการทำแบบทดสอบ Thai Montreal Cognitive Assessment (MoCA) และตอบแบบสอบถาม โดยผู้ที่ได้คะแนน MoCA <25 คะแนน จะได้รับการวินิจฉัยว่าเป็นภาวะพุทธิปัญญาเสื่อมระยะแรก (mild cognitive impairment, MCI) ปัจจัยที่เกี่ยวข้องกับภาวะพุทธิปัญญาเสื่อมจะได้รับการวิเคราะห์ทางสถิติโดยใช้โปรแกรมสำเร็จรูป SPSS 17.0 ด้วยวิธี Student t-test, Chi-square test และ multiple regression analysis

ผลการศึกษา: การศึกษานี้พบผู้ที่ได้รับการวินิจฉัยเป็นภาวะพุทธิปัญญาเสื่อมระยะแรกร้อยละ 43.5 การวิเคราะห์โดยวิธี univariate พบว่า ปัจจัยที่สัมพันธ์กับภาวะพุทธิปัญญาเสื่อมระยะแรกอย่างมีนัยสำคัญ ประกอบด้วย สถานภาพสมรส ระดับการศึกษา อาชีพ รายได้ต่อเดือน และระยะเวลาที่ได้รับฮอร์โมนทดแทน แต่เมื่อวิเคราะห์ด้วยวิธี multiple regression พบว่า ปัจจัยที่สัมพันธ์กับภาวะนี้มีเพียงอายุที่มากเมื่อเข้าร่วมการศึกษา สถานภาพสมรส ระดับการศึกษาที่ต่ำ และรายได้ต่อเดือนที่ต่ำสัมพันธ์กับภาวะพุทธิปัญญาเสื่อมระยะแรกอย่างมีนัยสำคัญทางสถิติ

สรุป: เกือบครึ่งหนึ่งของสตรีที่ได้รับการตัดรังไข่ทั้งสองข้างในการศึกษานี้ พบว่ามีภาวะพุทธิปัญญาเสื่อมระยะแรก ปัจจัยที่สัมพันธ์กับภาวะนี้อย่างมีนัยสำคัญประกอบด้วย อายุที่มากเมื่อเข้าร่วมการศึกษา สถานภาพสมรส ระดับการศึกษาที่ต่ำ และรายได้ต่อเดือนที่ต่ำ การศึกษานี้ไม่พบความสัมพันธ์ระหว่างอายุที่หมดระดูจากการตัดรังไข่ทั้งสองข้าง การได้รับฮอร์โมนทดแทนและภาวะพุทธิปัญญาเสื่อมระยะแรก