The Relationship between the Category of Menopausal Age Aand the Incidence of Stroke

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Abstract : The Menopause is associated with an increased risk of stroke. The decrease in estradiol at the early menopausal age can be detrimental to the health of blood vessels. The accumulation of risk factors occurring in menopause may be due to the excess of androgen and decreasing of estrogen, and mean to the twice of risk of stoke at 10 years after menopause. This study is a case control study conducted on patients treated at the Department of Neurology RSUPH. Adam Malik Medan after adjustment to the risk factors, all subjects will patients. The mean age for the case group was 58.51 (SD 8.119) years and was 61.80 (SD 8.860) years for the control group. In the case group the mean menopausal age 48.03 (SD 3.302) years was found in the control group and the mean menopausal age was 48.94 (SD 3.402) years.   The result of statistical analysis using Chi square test found no significant relationship between age category of menopause with stroke incidence.

Key words : menopausal age, stroke, risk factors, estrogen.

Introduction

Stroke is the second commonest cause of death and adult disability worldwide. Despite the advent of treatment that being selected in patients with stroke, the best approach to reduce the burden of stroke remains prevention.[1,2] Excess stroke in women at high age may arise from longer life expectancy and reaching ages of highest stroke risk compared with men.[3,4]   Since the sex differences in stroke began to be recognized, the particular influence of estrogen and testosterone on the endothelium and the vascular system, the role of risk factors to the women such as the use of oral contraceptives, hormone replacement therapy and pregnancy, the systemic delays in the recognition and insufficient treatment of conventional stroke risk factors in women have all been considered as probable explanations.[5]

The most common biological explanation for the protection of women against stroke is related to sex steroid hormone, especially estrogen. Several studies show that women are protected by endogenous estrogens.[6,7,8] In Hurn's study, estrogen has been widely shown to acutely protect brain from experimental

stroke.[9,10] Endogenous, or naturally occurring, estrogen production declines during menopause.[11,12] During perimenopause, estradiol levels decline by about 60%. After menopause, estradiol levels continue to decline but then plateau after one to three years.[13]

Early menopause is a significant predictor of future stroke and coronary heart disease in studies in multiethnic female populations in America, independent of common cardiovascular risk factors. [14,15,16]Early menopause is generally considered to occur when the last normal menstrual period occurs in the fourth decade.[17]Wellons's study shows that early menopause is associated with an increased risk of stroke.[14] In addition, the study from Rocca (2012) showed that 21% increased risk of all stroke mortality for women with younger age at menopause (≤ 44 y vs ≥ 51 y), regardless of the type of menopause (natural vs induced).[18]Women with menopause before age 42 had twice the risk of ischemic stroke compared to all other women, while women with menopausal age 42 - 54 years and menopausal age ≥ 55 years have a lower riskischemic stroke is relatively uncommon among premenopausal women, but the risk increases with age.[19,20]

Materials and Methods

This research is retrospective analytic with case control with matching as the data collecting method. The population of the present study consisted of 130 consecutive participants. The subjects were taken from stroke and non stroke patients who treat theirselves to the Polyclinic Neurology of Haji Adam Malik Hospital, Medan, Indonesia. The determination of research subjects was conducted according to non random sampling method on a consecutive basis.

As a case group, taken from stroke patients and had menopause who had treatment at the Neurology Polyclinic of Haji Adam Malik Hospital, Medan, Indonesia, and has been established with anamnesis, neurological examination and Head CT Scan examination head taken consecutively and who meet the criteria inclusion and no exclusion criteria and adjustments were made to Diabetes Mellitus risk factors, hypertension, migraine and smoking. As a control group, it was taken from non stroke patients who had menopausal treatment in Neurology Polyclinic of Haji Adam Malik Hospital, Medan, Indonesia on a consecutive basis and who fulfilled the inclusion criteria and there was no exclusion criteria and made matching risk factors for DM, hypertension, migraine and smoking. Patients who have age information at menopause and give consent to participate in this study were included in the study. Patients with decreased awareness and patients with aphasia were excluded.

Result

The total sample size is 130 people, consisting of 65 cases and 65 controls. The mean age for the case group was 58.51 (SD 8.119) years and was 61.80 (SD 8.860) years for the control group. Subjects from different ethnic groups were Bataknese 47 person (72.3%) in the case group and 49 (75.4%) in the control group. In the case group and control group most of the work is housewife. In both groups, education is mostly high school. In the case group the mean menopausal age 48.03 (SD 3.302) years was found in the control group and the mean menopausal age was 48.94 (SD 3.402) years. Characteristic demographic of the population are shown in Table 1.

Table 1. Demographic characteristics of research subjects

Characteristics of the subject	Case n= 65	Control= 65	*p*
Age, Mean (SD)	58.51±8.119	61.80±8.860	0.029*

Ethnic
  Batak
  Jawa
  Melayu
  Padang
  Aceh
	47 (72.3%)
	10 (15.4%)
	3 (4.6%)
	4 (6.2%)
	1 (1.5%)
		49 (75.4%)
		10 (15.4%)
		1 (1.5%)
		3 (4.6%)
		2 (3.1%)
			1.000***

Occupation Housewifey Civil servant Entepreur Farmer	44 (67.7%) 12 (16.5%) 4 (6.2%) 5 (7.7%)	53 (81.5%) 12 (18.5%) 0 (0) 0 (0)	0.562***
Education Elementary Junior High Senior High College	12 (18.5%) 13 (20.0%) 28 (43.1%) 12 (18.5%)	5 (7.7%) 15 (23.1%) 35 (53.8%) 10 (15.4%)	0,263**
Menopausal Age	48.03 (SD 3.302)	48.94 (SD 3.409)	0.126*
Type of Stroke Ischemic Stroke Hemorrhagic stroke	51 (78.5) 14 (21.5)	0 0	

* Mann Whitney Test,   ** Chi square Test,   ***Kolmogorov-smirnov Test, $p < 0,05$

Based on the menopausal age category of all 130 subjects, there were 11 subjects (16.9%) who had menopause at age 44, 41 subjects (63.1%) with menopausal age 45-50 years, and 13 subjects (20%) with menopausal age $\geq$ 51 years. For the control group there were 9 subjects (13.8%) with menopausal age $\leq$ 44 years, 37 subjects (56.9%) with menopausal age 45-50 years, and 19 subjects (29.2%) with menopausal age $\geq$ 51 years.

The relationship between the category of menopausal age and the incidence of stroke are shown in Table 2. The result of statistical analysis using Chi square test found no significant relationship between age category of menopause with stroke incidence ($p = 0.465$).

Table 2. The relationship between the category of menopausal age and the incidence of stroke

Menopausal Age	Case (%)	Control (%)	*p*
$\leq$ 44 years old	11 (16.9)	9 (13.8)	0.465
45-50 years old	41 (63.1)	37 (56.9)	
$\geq$ 51 years old	13 (20.0)	19 (29.2)	

*Chi square Test

Table 3 shows the greatest risk of menopausal age categories for the occurrence of stroke. It was found that the large odds ratio of menopausal age category did not significantly correlate with stroke incidence, with OR values being OR 0.6 (95% 0.2-1.73), OR 0.6 (95% 0.27-1.42).

Tabel 3. The Odd risk (OR) category of menopausal age with the incidence of stroke

Age category of menopause	Case (%)	Control (%)	OR (CI 95%)
$\leq$ 44 years old	11 (55)	9 (45)	0.6 (0.2-1.73)
45-50 years old	41 (52.6)	37 (47.4)	0.6 (0.27-1.42)
$\geq$ 51 years old	13 (40.6)	19 (59.4)	Comparison

*CI (confidence interval)

Discussion

This study is a retrospective analytical study with a case-controlled data collection method with matching, in order to know the odds ratio of the category of menopausal age to the incidence of stroke.

The total sample size is 130 people, consisting of 65 cases and 65 controls. The mean age for the case group was 58.51 ± 8.119 years and 61.80 ± 8.860 years for the control group. Subjects from different ethnic groups were Bataknese (47) (72.3%) in the case group and 49 (75.4%) in the control group. In the case group

and control group most of the work is housewife. In both groups, education is mostly high school. In the case group the mean age of menopause 48.03 (SD 3.302) years was found in the control group and the mean menopausal age is 48.94 (SD 3.402) years.

In this study found no significant relationship between the age category of menopause with the incidence of stroke, ischemic stroke or hemorrhagic stroke. This result is consistent with some previous studies. According to OR results obtained in this study on all stroke events, the value of OR is smaller than 1 or include the number 1. This result indicates that the age of menopause is not as a risk factor of the incidence of stroke.

This can be happen for reasons that the age of menopause is a less common risk factor in the incidence of stroke in both ischemic stroke and hemorrhagic stroke. In the study of Lisabeth et al in 2009 and Jacobsen et al in 2004 found that the percentage of menopausal age as a risk factor for stroke is only a few that is 4-5%.[19] Likewise with women who experience early menopause age is also a small amount. As in this study, women with menopausal age ≤ 44 years were 20 subjects (15%) of both groups.

The reason for the increased risk of stroke in women with early menopause is not very clear, but the early loss of ovarian function coupled with prolonged low estrogen states is a sensible hypothesis. Lisabeth et al's 2009 study shows that the relationship between menopausal age and stroke risk can be mediated through risk factor changes that occur in menopause, where there is an increase in some risk factors from stroke.[14]

To date, no studies have examined the relationship between endogenous estrogen and stroke hormones in premenopausal women or in women in menopausal transition to directly test this theory. Studies investigating the relationship between endogenous hormone estrogen and stroke are limited to postmenopausal

In conclusion, there was no significant relationship between menopausal age category and risk of stroke, ischemic stroke and hemorrhagic stroke.

References

1. Hanchaiphiboolkul S., Poungvarin N., Nidhinandana S., Suwanwela N.C., Puthkhao P., Towanabut S., et al., Prevalence of stroke and stroke risk factors in Thailand: Thai Epidemiologic Stroke (TES) study,J Med Assoc Thai., 2011, 94(4), 427-436.
2. Bilic I., Diamanja G., Lusic I., Matijaca M., Caljkusic K., Risk Factors And Outcome Differences Between Ischemic And Hemorrhagic Stroke, Acta Clin Croat, 2009, 48, 399-403.
3. Haast M.A.R., Gustafson R.D., Kiliaan J.A., Sex differences in stroke, J Cereb Blood Flow Metab, 2012, 32(12), 2100–2107.
4. Koellhoffer C.A. and McCullough D.L., The Effects of Estrogen in Ischemic Stroke, Transl Stroke Res, 2013, 4(4), 390–401.
5. Petrea R.E., Beiser S., Seshadri S., Kelly-Hayes M., Kase C.S., Wolf P.A.,Stroke in women - gender differences in stroke incidence and post- stroke disability in the Framingham heart study, Stroke, 2009, 40(4), 1032–1037.
6. Reeves M.J., Bushnell C.D., Howard G., Gargano J.W., Duncan P.W.,Lynch G., et al, Sex differences in stroke: epidemiology, clinical presentation medical care, and outcomes, Lancet Neurol, 2008, 21–23.
7. Griggs M.R. and Bluth I.E., Noninvasive Risk Assessment for Stroke: Special Emphasis on Carotid Atherosclerosis, Sex-Related Differences, and the Development of an Effective Screening Strategy, AJR, 2011, 196, 259 –264.
8. Hsieh Y-C., Hwang L-C., Hsieh F-I., Lien L-M., Lin H-J., Hu C-J., Tseng H-P., Bai C-H., Chiou H-Y., Early Menarche And Ischemic Stroke Risk Among Postmenopausal Women, International Journal of Gerontology, 2010, 4(1), 16-22.
9. Hurn D.P. and M. Brass M.L., Estrogen and StrokeA Balanced Analysis, Stroke, 2003, 34, 338-341.
10. Turtzo C.L and McCullough D.L., Sex Differences in Stroke, Cerebrovasc Dis, 2008, 26(5), 462–474.
11. Lee S.J., Yaffe K., Lui L-Y., Prospective Study of Endogenous Circulating Estradiol and Risk of Stroke in Older Women, Arch Neurol, 2010, 67(2), 195-201.
12. Yasui T., Matsui S., Tani A., Kunimi K, Yamamoto S., Irahara M., Androgen in postmenopausal women, The Journal of Medical Investigation, 2012, 59, 12-27.

13.   BushnellC.D., Stroke in Women: Risk and Prevention Throughout the Lifespan, Neurol Clin, 2008, 26(4), 1161–xi.

14.   Wellons M., Ouyang P., Schreiner P.J., Herrington D.M., Vaidya D., Early Menopause predicts future coronary heart disease and stroke: The multi-ethnic study of atherosclerosis, Menopause, 2012, 19(10), 1081-1087.

15.   Jacobsen K.B., Heuch I., Kvåle G., Age at Natural Menopause and Stroke Mortality Cohort Study With 3561 Stroke Deaths During 37-Year Follow-Up, Stroke, 2004, 35, 1548-1551.

16.   Wu X., Cai H., Kallianpur A., Gao Y-T., Yang G., Chow W-H., Li H-L., Zheng W., Shu X-O., Menarche and Natural Menopause and Number of Reproductive Years in Association with Mortality: Results from a Median Follow-Up of 11.2 Years among 31,955 Naturally Menopausal Chinese Women, Menstrual and Reproductive History and Mortality, 2014, 9(8), 1-10.

17.   Baba Y., Ishikawa S., Amagi Y., Kayaba K, Gotoh T., Kajii E., Premature menopause is associated with increased risk of cerebral infarction in Japanese women, Menopause: The Journal of The North American Menopause Society, 2010, 17(3), 506-510.

18.   Rocca W.A., Grossardt B.R., Miller V.M., Shuster L.T., Brown Jr R.D., Premature menopause or early menopause and risk of ischemic stroke, Menopause, 2012, 19(3), 272–277.

19.   Lisabeth L. and Bushnell C., Menopause and stroke: An epidemiologic review, Lancet Neurol, 2012, 11(1), 82–91.

20.   Alonso de Lecinana M., Egido J.A., Ferna´ndez C., Martı´nez-Vila E., Santos S., Morales A., Martı´nez E., Pareja A., lvarez-Sabı´n J.A., I. Casado., Risk of ischemic stroke and lifetime estrogen exposure, Neurology, 2007, 68, 33-38.

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