Original article

Correlation between Digit Ratio and Incidence of Meningioma and its Clinical Profiles

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Abstract

Background: Proliferation and progression of meningioma were influenced by the balance of estrogen and testosterone. Digit Ratio (DR) was a sign of prenatal exposure to estrogen and testosterone. This study intends to find the relationship between Digit Ratio and meningioma. ***Aim:*** To determine the relationship between DR and incidence of Meningioma and its Clinical Profiles (age at the onset, sex, Body Mass Indec (BMI) and histopathology grading***) Methods:*** Analytical observational study was used with case-control design. Case group consisted of patients clinically and histopathologically diagnosed with meningioma (n=25). Patients who were not diagnosed with primary intracranial tumors were included in the control group (n=25). Matched group were conducted. Subjects of this study were patients of RSUP dr Kariadi in the period of January 2016-August 2017. This study was conducted by collecting data consisted of DR, age, sex, BMI, and grading histopathology. Tests used in this study are Chi-Square Test, Mann-Whitney Test and Fishers exact Test. ***Results:*** Digit Ratio Mean for right, left and right-left difference were 1.0041; 1.0104 and 0.0357 while for the right and left DR cutoff value 0.993; 0.989. There is a relationship between right and left Digit Ratio and incidence of meningioma (p = 0,000) with OR (Odds Ratio) Right DR = 11.17(CI95% 2,864 – 43,464) and OR left DR = 16,00 (CI95% 4,002 – 63,975). There is a relationship between Right Digit Ratio andBMI case group (p = 0,022). There is no relationship of Digit Ratio and age at onset, gender and histopathology grading (p <0.05). ***Conclusion:*** DR is risk factor of Meningioma

Keywords: Meningioma; Digit Ratio

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Introduction

Meningioma is the primary intracranial benign tumor which is originates from the pia tissue and arachnoid [1]. Meningioma is associated with Body Mass Index (BMI). Meningioma is also associated with high estrogen, progesterone, androgen activity and insulin-like growth factor.[4] Recent studies investigated the impact of prenatal exposure of steroid hormones corelates to the ratio of finger length. Measurement of Digit Ratio (DR), or more precisely the Second-to-Fourth (2D: 4D) ratio, which is a sign of exposure to testosterone and prenatal estrogen and increased sensitivity to testosterone and esterogen[6]. In patients with a history of high estrogen exposure in prenatal, it will increase the sensitivity of some related receptors. Among them are Estrogen Receptor (ER), Progesterone Receptor (PR), and Fibroblast Growth Factor Receptor 1 (FGFR1).[7,8] The relationship between DR to the incidence of Meningioma and its clinical profile were elucidated.

Method

This was an observational analytic study with case-control study design. One group was a group of patients diagnosed with meningioma and one group was people without meningiomas with the same characteristics as the case group selected by

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matching method. The data taken were the primary data. Consecutive sampling was conducted. The independent variable was DR. The dependent variables were the incidence of meningioma and its clinical profile, which consisted of age at the onset of symptoms, BMI, gender and histopathologic Grading.

Ethical Clearance: This study was approved by ethics Committee of Diponegoro University.

Results

The numbers of samples obtained from July to September were 50 samples with 25 samples of meningioma patients included in the case group and 25 samples of patients diagnosed in addition to Meningioma that included inclusion criteria and excluded exclusion criteria

Table 1. Characteristics of research subjects (categorical)

	Case		Control	
	n	%	n	%
Gender				
• Man	3	6,0	3	6,0
• Woman	22	44,0	22	44,0
Total	25	50,0	25	50,0
BMI				
• Underweight	1	4,0	4	16,0
• Normoweight	7	28,0	7	28,0
• Overweight	17	68,0	14	56,0
Total	25	100,0	25	100,0
Histopathological Grading WHO				
• Grade I	10	40,0	-	-
• Grade II	14	56,0		
• Grade III	1	4,0		
Total	25	100,0		

Table 2. Characteristics of research subjects (numerical)

	Case		Control	
	Median (Minimum-Maximum)	Average (standard deviation)	Median (Minimum-Maximum)	Average (standard deviation)
Age				
• **Age**	45 (20-62)	43,92(7,472)	47(20-60)	42,32(11,242)
Age at Symptoms	43(19-58)	42,36(7,076)	-	-

Based on the age characteristic, the case group, the youngest age was 20 years old and the oldest was 62 years with the average age of 43.92 years. In the control group, the youngest age was 20 years old and the oldest was 60 years with the average age of 42.32 years. Thus, it was concluded that case and control groups were matched groups for gender and age.

Results of Digit Ratio Measurement

Table 3. Measurement Digit Ratio

	Case			Control		
	Median (Minimum-Maximum)	Average (Standard Deviation)	CL95%	Median (Minimum-Maximum)	Average (Standard Deviation)	CL95%
DR Right	1,0082(0,8977-1,0979)	1,0041(0,0438)	0,9860-1,0222	0,9703(0,8763-1,0584)	0,9712(0,0473)	0,9517-0,9908
DR Left	1,0116(0,9343-1,0971)	1,0104(0,0333)	0,9967-1,0242	0,9597(0,8259-1,0519)	0,9556(0,0553)	0,9327-0,9784
Deferace of DR	0,0230(0,0026-0,1259)	0,0357(0,0340)	0,0216-0,0498	0,0511(0,0018-0,1546)	0,0540(0,0421)	0,0366-0,0714

Table 4. Hypothesis test of categorical variables

Test			Groupn(%)				Score *p Right*	Score *p Left*
			DR Right		DR Left			
			>0,993	<0,993	>0,989	<0,989		
Meningioma Incidence	*Chi-Square*	Meningioma	17(81,0)	8(27,6)	20(80,0)	5(20,0)	0,000*	0,000*
		Not Meningioma	4(19,0)	21(72,4)	5(20,0)	20(80,0)		
BMI (case)	*Mann-Whitney*	Underweight	1(5,9)	0(0,0)	1(5,0)	0(0,0)	0,002*	0,096
		Normoweight	7(41,2)	0(0,0)	7(35,0)	0(0,0)		
		Overweight	9(52,9)	8(100)	12(60,0)	5(100,0)		
BMI (control)	*Mann-Whitney*	Underweight	1(25,0)	3(14,3)	1(20,0)	3(15,0)	0,619	0,939
		Normoweight	0(0,0)	7(33,3)	1(20,0)	6(30,0)		
		Overweight	3(75,0)	11(52,4)	3(60,0)	11(55,0)		
Gender (case)	*Fishers Exact*	Man	2(11,8)	1(12,5)	2(10,0)	1(20,0)	0,704	0,546
		Woman	15(88,2)	7(87,5)	18(90,0)	4(4,0)		
Gender (control)	*Fishers Exact*	Man	0(0,0)	3(14,3)	0(0,0)	3(20,0)	0,578	0,496
		Woman	4(100,0)	18(85,7)	5(100,0)	17(85,0)		
WHO Grading Histopatology	*Mann-Whitney*	Grade I	8(47,1)	2(25,0)	9(45,0)	1(20,0)	0,423	0,414
		Grade II	8(47,1)	6(75,0)	10(50,0)	4(80,0)		
		Grade III	1(5,9)	0(0,0)	1(5,0)	0(0,0)		

*p<0,05

Table 4. Hypothesis test of categorical variables

			Mean Rank	*p*
Case	***Digit Ratio*Right Score**	>0,993	27,48	0,414
		<0,993	24,07	
	Digit Ratio Left Score	>0,989	25,94	0,831
		<0,989	25,06	

TheOR of Digit Ratio Right to the occurrence of meningioma was 11.17 with confidence level 95% 2,864 - 43,464. It was found that the sample with the right Digit Ratio value> 0.993 has 11.17 times for the occurrence of Meningioma compared with the sample with the value of Digit Ratio left <0.993

Discussion

Digit Ratio is the ratio of finger length to second and fourth finger[32]. In clinical examination there were 3 parameters of DR, DR Right, DR Left, and Difference DR.[9]

In previous research, the researcher got cutoff point value of DR 0,950.[37]. While in this research, we got cutoff point value for right DR, Left and difference of each digit were 0,993, 0,989, and 0,030.

The results of comparative categorical test by Chi-Square Test showed significance p = 0,000 (p

<0.05) for the right Digit Ratio relationship to the occurrence of meningioma, p = 0,000 (p <0.05) for the relationship Digit Ratio left against the incidence of meningioma.

In theory, the Digit Ratio value shows the prenatal balance of estrogen and progesterone. In the study, it was concluded that the value of right and left Digit Ratio over the value of cutoff point has a higher risk for experiencing meningioma. It is in line that the Digit Ratio value of more than 1 has a higher prenatal estrogen tendency[38]. Whereas in Meningioma, one of the tumor developments is affected by the balance of reproductive hormones, especially high estrogen[39]. Furthermore, in histopathology review, ER + was obtained in patients with Meningioma. This is associated with a Digit Ratio value greater than 1 and above the cutoff point in this study.[16]

In the whole group and control group, there was no significant correlation between Right Digit Ratio to BMI p = 0,619 (p> 0,05). While in the group of meningioma patients, there was a significant correlation between Right Digit Ratio and BMI p = 0,022 (p <0,05). This is in line with research conducted by Magdalena which concluded that the relationship of Digit Ratio to BMI.[30]

In Digit Ratio left and Difference of Digit Ratio to BMI in all group, case group and control group there is no statistically correlation (p> 0,05). This is influenced by many factors, including Meningioma itself as a chronic disease, nutritional intake, genetic, and stress levels[30]. And in this study, these confounding factors were not the focus of the study.

In this study, there was no correlation between Right Digit Ratio, left and gender difference in all group, case group and control with p> 0,05.

From epidemiological data, female does have prevalence more often than male[14]. However, in this study there is no relationship between the two. This could be due to a sample of only 50 and unequal gender distribution.

In this study, the proportion of WHO Histopathology Grading was 40.0% for Grade I, 56.0% for Grade II, and 4.0% for Grade III. This is in line with that of Meningioma in general are Grade I and Grade II. [11]

From the test, obtained p> 0,05 for relationship of Digit Ratio right, left and difference to WHO histopathology Grading. Hence, there is no relationship between Digit Ratio right, left and Difference Digit Ratio to WHO histopathology grading.

In this study, it has not proven ER/PR attachment to WHO Histopathology. Meanwhile, ER and PR are among the factors that explain that the tumor is responsive to estrogen/progesterone.[11] Digit Ratio is also directly related to prenatal estrogens suspected to be associated with ER profiles in histopathologic preparations of patients with meningioma.

From this study, use numerical analysis of age values when symptoms appear on Digit Ratio. Results obtained p> 0.05 for Digit Ratio right, left, and the difference Digit Ratio to age when symptoms appear. Thus, it is concluded that there is no relationship between digit ratio right, left digit ratio and difference on the patient's age when symptoms appear. This is in contrast to previous research which states that the lower the Digit Ratio value, the older age of the patient when the symptoms appear.[9]

From the calculation of Odds Ratio (OR) the Right Digit Ratio to the incidence of meningioma is 11.17 and the Left Digit Ratio to the occurrence of meningioma is 16.00. It is known that the sample with the right Digit Ratio> 0.993 has a possible risk of 11.17 times the occurrence of Meningioma. Then, the sample with the left digit> 0.989 has a 16 chance risk of meningioma. This possibility is caused because Meningioma is one of the tumors that are sensitive to estrogen[40]. The process of formation and growth of the tumor mass is influenced by estrogenic circulation. In patients with a Digit Ratio greater than 1 have a predisposition for dominant prenatal estrogen, and this is associated with the incidence of meningioma.[31]

In this study, weight and height measurements were taken when patients were still able to be co-operated, in patients with impaired awareness and limb disability, weight and height data were taken at the time of admission to the hospital seen from medical records. Then, the difference in measuring instruments used (the scales on the wards, the scales at the emergency room, and the scales brought by the researcher for home visits) is also one of the limitations of this study. This study, only explaining the presence or absence of relationships and the magnitude of risk factors, but cannot explain why it can affect each other. It is hoped that further research with regard to ER histopathology of meningioma can be a bridge connecting Digit Ratio relation to meningioma occurrence.

This study also used consecutive sampling due to the small prevalence of cases and limited time of research. In subsequent research, it is desirable to use sampling methods that better represent actual populations.

Conclusions and suggestions

Conclusion

Based on the results of research that has been discussed, it was found that the DR is a risk factor of Meningioma.

Suggestion

Based on the conclusions of this study, the researcher gives suggestions for the next research, it is expected to improve the short comings of this study, among others, increasing the number of samples and length of research. Then, in this study, only explains the relationship without explaining the cause of each variable. The next researcher is expected to strengthen the result of this research by perfecting the research method.

Authors' Contribution:

Data gathering and idea owner of this study: Brilliantika SP, Arifin MT, Istiadi H

Study design: Brilliantika SP, Arifin MT

Data gathering: Brilliantika SP, Arifin MT, Istiadi H, Winarni TI, Muhartomo H

Writing and submitting manuscript: Brilliantika SP, Arifin MT

Editing and approval of final draft: Brilliantika SP, Arifin MT, Istiadi H, Winarni TI, Muhartomo H

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