

Journal of Society Medicine Research & Review Articles on Diseases

Journal of Society Medicine. 2023; 2(7)

Evan's Index Values and Its Relationship with Individual Characteristics (Age and Gender) in Head CT-Scan Examination at Haji Adam Malik Hospital Medan 2021-2022

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ARTICLE INFO	ABSTRACT
Andiala bindamu	Introduction: Enlargement of the ventricles caused by disturbances in the production,
Article history: Received	flow, and absorption of cerebrospinal fluid is known as hydrocephalus.Radiological
21 June 2023	examinations such as computed tomography (CT) play an important role in establishing
	the diagnosis of hydrocephalus. Assessment of ventricular enlargement in most cases is
Revised	done subjectively and based on radiological experience. Objectively, ventricular size can
01 July 2023	be assessed by linear ratios on CT. Evan's index (EI) is the simplest and most reliable
Accepted	method for assessing ventricular size. Age and sex have an influence on the size of the
31 July 2023	ventricles. The aim of this study was to determine the average Evan's Index and its
	relationship with individual characteristics (age and sex) in patients who underwent head
Manuscript ID: JSOCMED-210623-27-3	CT scans at H. Adam Malik General Hospital, Medan.
JSOCWIED-210025-27-5	Method: This study used a case series design to determine the relationship between
Checked for Plagiarism: Yes	individual characteristics (age and gender) with the Evan's Index value and to obtain an
	average normal Evan's Index value in patients who underwent head CT scans at the Haji
Language Editor: Rebecca	Adam Malik General Hospital in Medan.
Kebecca	Results: The highest sample age was in the 19-30 year age group, namely 39 people
Editor-Chief:	(35%). In this study, there were more female subjects, namely 51% compared to males
Prof. Aznan Lelo, PhD	(49%). Mean + standard deviation and median (min-max) in Evan's Index data were 0,26
	+ 0,03 and 0,25 (0,2-0,36). There was a significant correlation between age and the
	Evan's Index ($p < 0.001$) with a moderate degree of correlation (0.442). There was no
	significant relationship between gender and Evan's Index (p=0,121; np2=0,022). There
	was no significant difference between education levels and the average Evan's Index
	(p=0.434).
	Conclusion: There is a relationship between the increase in the age group of the
	participants and the increase in the EI value which is linear and correlative. There was
	no difference in EI values between gender and level of formal education regardless of
	the age group of the individuals analyzed.
Keywords	Evan's Index Values, Head CT-Scan Examination, Ventricular Size
	<i>How to cite</i> : Zamzami MA, Daulay E, Indharty S. Evan's Index Values and Its Relationship with Individual Characteristics (Age and Gender) in Head CT-Scan Examination at Haji Adam Malik Hospital Medan 2021-2022. <i>Journal of Society Medicine</i> . 2023; 2(7): 232-240. DOI: https://doi.org/10.47353/jsocmed.v2i7.69

INTRODUCTION

The cranial cavity contains the brain, blood vessels, and cerebrospinal fluid (CSF), which is mostly in the ventricular system. The ventricular system of the central nervous system is responsible for transporting the cerebrospinal fluid produced by the ependymal cells and the choroid plexus. The ventricular volume accounts for 2% of the brain volume [1].

Enlargement of the ventricles caused by disturbances in the production, flow, and absorption of cerebrospinal fluid is known as hydrocephalus. In Indonesia, the incidence of hydrocephalus reaches 10 per mil. In global cases, the overall prevalence of hydrocephalus in the world reaches 85 per 100,000 [1].

For the diagnosis of hydrocephalus, apart from clinical examination, radiological examinations such as computed tomography (CT) play an important role. CT scan is a widely used and relatively affordable modality for imaging the brain. Assessment of ventricular enlargement in most cases is done subjectively and based on radiological experience. Objectively, ventricular size can be assessed by linear ratios on CT. Evan's index (EI) is the simplest and most reliable method for assessing ventricular size. Sherman et al. states that the normal value of EI is <0.3 [2,3]. EI is the ratio of the transverse diameter of the anterior horn of the lateral ventricle to the largest internal diameter of the cranium at the level of the foramen of Monro, which is used in axial CT and MRI projections, and has been widely used as an indirect marker of ventricular volume. Age and sex have an influence on the size of the ventricles [3,4].

There are no studies in Indonesia that have assessed ventricular size in healthy individuals and examined its relationship with age and sex. Therefore, researchers used the Evan's index (EI) to assess ventricular size with a CT scan imaging modality. This study was conducted to determine the average Evan's Index and its relationship with individual characteristics (age and sex) in patients who underwent head CT scans at H. Adam Malik General Hospital, Medan. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) asserts that headaches are one of the major public health concerns globally.[1] Headache is the most prevalent neurological symptom which can be of a serious condition, as in brain tumor, however it is generally a benign condition that includes primary headache such as migraine or tension-type headache (TTH).[2]

Globally, the prevalence of tension-type headache (TTH) is greater than that of the other headaches.2 In accordance with the 2016 Global Burden of Disease (GBD), approximately three billion people suffer from TTH and migraine worldwide, of which 1,89 billion suffer from TTH.[3] In a study on the prevalence of TTH in various countries, the highest TTH is in Indonesia.[3] The incidence of tension-type headache (TTH) in Indonesia is around 23.000 to 27.000 per 100.000 population, while on Sumatra Island, there are 25.000 to 27.000 people experiencing tension-type headache per 100.000 population.[4]

Fatigue is a common symptom that is potentially debilitating and impacts the health-related quality of life of individuals diagnosed with acute and chronic medical conditions.[5] The global prevalence of fatigue varies between 2,36-75,7%. The wide prevalence range value is due to the absence of gold standard test for fatigue, so there are differences in definitions, measuring instruments, and measurement methods. In a study conducted on anaesthesia resident doctors working at RSCM in 2018, it was reported that 55,6% experienced fatigue.[6] Residency training has a difficult and stressful developmental phase in professional careers. Residents often experience prolonged working hours, prolonged sleep deprivation, uncontrollable schedules, high job demands, and inadequate private-time. These can lead to burnout, which is characterized by emotional exhaustion, depersonalization, and decreased personal achievement. Besides, the residency can affect quality of life and cause sleep disorders, family issues, and even psychiatric disorders.[7]

METHOD

This study used a case series design to determine the relationship between individual characteristics (age and gender) with the Evan's Index value and to obtain an average normal Evan's Index value in patients who underwent head CT scans. The study was conducted at the Haji Adam Malik General Hospital in Medan after passing Ethical Clearance by collecting data from head CT scans until the minimum number of samples was met. This research starts from August 2022-October 2022.

The study population was patients who had undergone head CT scans and the CT scan results were stored in the database. The research sample was part of the study population that meets the inclusion and exclusion criteria. The technique of obtaining samples was by consecutive sampling, where samples are taken sequentially according to the inclusion and exclusion criteria until the minimum size was met. The inclusion criteria for this study were patients aged >18 years, with normal head CT scan findings [5]. While the exclusion criteria were patients with incomplete, missing, or inaccessible medical record data; there is a motion artifact on the CT scan; a very asymmetrical CT scan; and CT scan with abnormal findings such as bleeding, intracranial SOL, impression fracture.

From the calculation results for a minimum sample size of 58 research subjects, however, in order to facilitate the inferential analysis to be carried out, 60 research subjects were recruited. After obtaining approval from the Ethics Committee of the Faculty of Medicine, Universitas Sumatra Utara, data was collected on the CT scan results of the head in the radiology database at the Radiology Department of Haji Adam Malik General Hospital Medan. After recording the results of the head CT scan, a search for patient data was carried out based on the medical record number that had been obtained from the previous data collection. Then, the patients were sorted based on the inclusion and exclusion criteria based on the medical record data obtained.

Patient data that met the inclusion and exclusion criteria were included in the study subjects and the age, sex, and results of the Evan's Index measurement were recorded by two readers. The patient's chief complaint as an indication for a CT scan was also recorded. Evan's Index (EI) was obtained on axial projection CT scan. Two of the readers are radiologists or radiology residents who have competence in assessing CT scan results. All data obtained was processed and analyzed statistically.

Data analysis was performed using statistical software. Subject clinical and demographic data including age, gender, and Evan's Index results. Data on a categorical scale will be displayed in percentage values and data on a numerical scale will be displayed in mean and standard deviation values, all data will be presented in tabular form. The data to be analyzed previously will be tested for uniformity between the two readers of the CT scan results using the Kappa test. Then an inferential analysis was performed to analyze the relationship between age and the Evan's Index using the Pearson correlation test if the data was normally distributed or with the Spearmann test if the data was not normally distributed. Inferential analysis was also performed to analyze the relationship between gender and the Evan's Index using the Eta test.

RESULT

There were 110 research subject data that met the inclusion and exclusion criteria. Although the calculation results for determining the sample size stated that the minimum sample required were 60 individuals, the researchers managed to obtain 110 eligible subject data for further analysis so that the research could be continued.

Demographic Data	Ν	%
Age		
19-30	39	35
31-40	14	13
41-50	16	15
51-60	26	24
61-70	8	7
>70	7	6
Gender		
Male	54	49
Female	56	51
Education Levels		
Elementary school	4	3,6
Middle school	3	2,7
High school	86	78,2
D3	2	1,8
Bachelor	15	13,6

Table 1. Demographic Data Characteristics

In Table 1, the highest sample age was in the 19-30 year age group, namely 39 people (35%), and the least age category was in the >70 year group, namely 7 people (6%). In this study, there were more female subjects, namely 51% compared to males (49%). In addition, it was also known that the highest education level in the sample was high school, amounting to 86 people (78.2%), and the education level of the least sample was D3, amounting to 2 people (1.8%).

Then an analysis was also carried out using the Kappa test to determine the uniformity between two readers (P1 = researcher; P2 = comparison) CT scan results using the Kappa test.

Data Type	Mean	SD	Median	Min	Max	Kappa	P-value
Evan's Index P1	41,86	17,49	43	19	90	0,776ª	<0.001ª
Evan's Index P2	0,26	0,03	0,25	0,2	0,36		

Table 2 Results of the Evan's Index Uniformity Analysis

^aKappa test

Based on Table 2, the analysis using the Kappa test shows that uniformity or consistency between two readers was significant (p<0.001) with a good degree of uniformity or consistency (p=0.776).

Table 3 Descriptive Data Analysis Results

Data Type	Mean	SD	Median	Min	Max	P-value
Age	41,86	17,49	43	19	90	<0,001 ^b
Evan's Index	0,26	0,03	0,25	0,2	0,36	<0,001 ^b
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^bKolmogorov-Smirnov normality test

Based on Table 3, it was known that mean + standard deviation and median (min-max) in the age data were 41,86 + 17,49 and 43 (19-90) and mean + standard deviation and median (min-max) in Evan's Index data were 0,26 + 0,03 and 0,25 (0,2-0,36). In addition, it was also known that the results of the normality test show that the age data and Evan's Index were not normally distributed. Data was declared normally distributed if the p-value of the normality test was > 0.05 and declared not normally distributed if the p-value of the normality test was <0.05.

Age Relationship Analysis with Evan's Index

In the analysis of the relationship between age and the Evan's Index, an analysis was carried out using the Spearmann test because from the normality test results it was known that the age data and the Evan's Index were not normally distributed. Based on Table 4, it was known that there was a significant correlation between age and the Evan's Index (p < 0.001) with a moderate degree of correlation (0.442).

Table 4 Age	Correlation	Test Results	with Evan	's Index
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	Data Type	Mean	SD	r	P-value
Age		41,86	17,49	0,442°	<0.0010
Evan's Index		0,26	0,03		<0,001°
^c Spearmann test					

Table 5 Age Group Difference Test Results with Evan's Index

	Age	Mean	SD	P-value
19-30 years		0,24	0,02	
31-40 years		0,25	0,02	
41-50 years		0,25	0,02	0.001d
51-60 years		0,27	0,03	0,001 ^d
61-70 years		0,27	0,04	
>70 years		0,30	0,03	

^dKruskal-Wallis test

In the analysis of age group differences with the Evan's Index, an analysis was carried out using the Kruskal-Wallis test because it was known from the results of the normality test that the Evan's Index data was not normally distributed. Based on Table 5, it was known that there was a significant difference between the age groups with an average Evan's Index (p < 0.001).

Gender Relationship Analysis with Evan's Index

The Eta test was carried out between the gender and the Evan's Index to find out the relationship between the two. The Eta test analysis was carried out and then continued with the ANOVA test to obtain Partial Eta Squared results to draw conclusions from the analysis results.

Table 6 Analysis Results of Gender Relations with Evan's Index

Data Type	Eta's Value	Partial Eta Squared	P-value
Gender	0.156 ^e	0,022 ^f	0,121 ^f
Evan's Index	0,130	0,022	0,121

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^eEta test fANOVA test

Based on Table 6 it was known that the Eta value was 0.156 after analysis with the Eta test, then continued with the ANOVA test to determine the results of Partial Eta Squared and it was known that there was no significant relationship between gender and Evan's Index (p=0,121; np2=0,022).

Education Levels Relationship Analysis with Evan's Index

In analyzing the differences in education levels with the Evan's Index, an analysis was carried out using the Kruskal-Wallis test because it was known from the results of the normality test that the Evan's Index data is not normally distributed. Based on Table 7, it was known that there was no significant difference between education levels and the average Evan's Index (p=0.434).

Table 7 Education Levels Difference Test Results with Evan's Index

Educat	tion Levels	Mean	SD	P-value
Elementary school		0,26	0,01	
Middle school		0,25	0,03	
High school		0,25	0,03	0,434 ^d
D3		0,25	0,02	
Bachelor		0,27	0,04	
dIZ				

^dKruskal-Wallis test

DISCUSSION

This study basically discusses whether there is a clinically significant correlation between age and gender of an individual on the Evan's index (EI) value based on the results of radiological imaging using head CT scans. Identification of the EI itself has a significant role considering the presence of the formula can serve as a radiological reference, whether there is enlargement of the lateral ventricles (which make up \pm 82% of the ventricular system in the brain), relative to the cranium. Thus, EI is often called the ventriculo graphic index, which, as mentioned in the introduction, is the ratio between the maximum width of the frontal horns of the lateral ventricles and the maximum diameter of the inner side of the skull [6,7]. The purpose of determining the size of the ventricles is to assist in establishing a diagnosis such as ventriculomegaly and/or hydrocephalus with symptoms that manifest in the patient's clinical setting. Considering that changes in the EI value itself are strongly influenced by intracranial pathology involving ventricular system malfunction (both as a cause and as a result), determining the normal limits of a parameter must of course be done by including the normal

population. Thus, this study included the adult population (> 18 years) with normal head CT scan results at the Haji Adam Malik General Hospital in Medan.

With an analytic-case series research design, this study analyzed 110 adult individuals (51.0% female), dominated by the age group 19-30 years (35.0%), followed by 51-60 years (24.0%), 41-50 years (15.0%), 31-40 years (13.0%), 61-70 years (7.0%), and >70 years (6.0%). Thus, the majority of individuals included in this study were from the productive age group, even though 33.6% of the participants were >50 years old, which in turn could serve as a comparison whether there were differences in EI values between the older and younger age groups. The majority of participants in this study only had education up to high school level (78.2%), followed by Bachelor (13.1%), Elementary School (3.6%), Middle School (2.7%), and D3 (1.8%). Analysis of the descriptive data that the researchers obtained showed that the mean age of the participants was 41.86 ± 17.49 years with a median value of 43 (19-90). On the other hand, the average EI value obtained was 0.26 ± 0.03 with a median value of 0.25 (0.20-0.36) for all participants included in this study. These results also show that both age and EI data in this study were not normally distributed after the Kolmogorov-Smirnov normality test was carried out.

The results of the correlative test between the independent variables (age & sex) and the dependent variable (EI) showed that there was a relationship with a moderate degree of correlation (0.442; P <0.001 with 95% CI) between the mean age of the study subjects and EI. Furthermore, analysis of the age group (19-30 years, etc. up to >70 years) showed the same results after being analyzed using the Kruskal-Wallis test. Meanwhile, the relationship between gender and EI reported did not show a statistically significant correlative aspect, with the results of the ANOVA test (Partial Eta Squared) having a value of 0.156 (0.022) and a P value of around 0.121 so that the results were considered not significant.

When compared with the literature and other previous studies by Arun et al., there was no significant difference in the EI value (P value = 0.161) between the male group (0.27 ± 0.04) compared to the female group (0.26 ± 0.03) . The same study also showed that there was a quantitative difference between the age group ≤ 20 years (0.24 ± 0.03) and ≥ 60 years (0.28 ± 0.03) even though no statistical correlative analysis was performed in the study [6]. Another study by Reddy et al. in 326 healthy individuals (mean age 41.34 ± 19.44 years) from India, the mean EI value obtained was 0.25 ± 0.02 , qualitatively similar to this study. However, Reddy et al. also stated that there was no significant difference between the young and old age groups e.g., 11-20 years vs. 21-30 years vs. 31-40 years and so on. up to age ≥ 91 years; although in the graph shown there is a difference in the average EI value of at least 0.05 in these studies [3]. Dzefi-Tettey in 2021 concluded a cut-off value that could theoretically be used as an average adult individual EI value, namely 0.24 ± 0.02 . Basically, the study studied 407 participants from Ghana with an average age of 48.29 ± 17.63 years. Both the male and female populations in the study had an EI value of 0.24 ± 0.02 so it was concluded that there was no statistically significant difference in the entire study. Furthermore, Dzefi-Tettey also mentioned that there were quantitative differences in the EI values in the younger age group (22-31 years with EI 0.219 ± 0.013 (female) and 0.221 ± 0.011 (male) compared to ages ≥ 72 years with EI 0.276 ± 0.011 (female) and 0.280 ± 0.009 (male) [5].

Therefore, three studies have consistently stated that there is no difference in EI values in the male and female groups so that it is suspected that gender does not have a significant effect on ventricular size. On the other hand, this study shows that there is an effect of different age groups on increasing EI values, with significant differences in values for each group, e.g., 19-30 years (0.24 ± 0.02) vs. 51-60 years (0.27 ± 0.03) or even when compared to the oldest age group (>70 years with an EI value of 0.30 ± 0.03). Thus, this study is quite related to several studies that have been used as comparisons regarding the results obtained in a certain population group.

The findings in the form of higher EI values in the older age group are very likely influenced by several crucial things related to the degeneration of the intracranial structures that occur. For example, a study by Brix et al. who compared relatively healthy elderly with elderly who had been diagnosed with Alzheimer's disease showed an average EI value of around 0.30 or more. To provide a deeper context regarding the elderly, the classification of these age groups based on their range is 65-74 years (group 1; youngest old), 75-84 years

(group 2; middle-old), and \geq 85 years (group 3; oldest old). Theoretically, patients in groups 2 and 3 will have a higher average EI value, as described in this study and some other reference literature. Another study by Dhok et al., proposed a cut-off value of around 0.34 for individuals aged >70 years. Differences between existing studies are thought to be influenced by ethnic and racial aspects of the population analyzed, with the study of Dhok et al., studying a group in central India and Brix et al., investigating a combined group from North America and Western Europe [8,9]. The results of the two studies are consistent with what the researchers got, namely individuals aged >70 years have relatively greater EI values than younger age groups. Another discussion regarding how high the EI value is in a group so that it can be said to be pathological is very general, discussing the optimal cut-off value. A study by Missori et al., in 2016 concluded that it is true that there is a higher EI value at an older age, but healthy individuals (without anatomical or physiological abnormalities) never reach the pathological cut-off value of EI, which in that study was considered about 0.30. Interestingly, Missori et al. also found a significant difference in EI values between the male (0.28 ± 0.04) and female (0.27 ± 0.04) populations with P value = 0.01 [10]. However, the theory that can confirm the difference in EI values between men and women is still not fully understood, moreover the findings of different EI values are more likely to be related to aspects of race/ethnicity of the population being studied.

It is important to understand that the influence of anatomical degeneration which will manifest clinically in an elderly person such as brain tissue atrophy and relative ventricular enlargement, will affect the findings of the EI value on a head CT scan; although the influence of the maximum width of the cranium can also affect the value of EI. Progressive ventricular enlargement correlates linearly with increasing age so that a value of 0.30 is often used as a cut-off to indicate the presence or absence of pathological ventricular enlargement in an individual. As a radiological marker, the role of EI itself is not limited to assessing the ventricular system, but may also reflect changes or decreases in brain mass that can occur in old age; moreover, there is a hypothesis which states that men may have a higher EI value even though this study did not find these results. In addition, the correlation between a history of head trauma and a diagnosis of other intracranial pathology is unclear, although a study by Poca et al. mentioned that there was a significant difference in EI values after moderate and severe acute head trauma [11].

The diagnosis of normal pressure hydrocephalus (normopressure hydrocephalus or NPH), which is increasingly common in the elderly population, can also be made on the basis of finding an EI value >0.3. The increase in ventricular volume accompanied by atrophy of brain tissue with increasing age will certainly increase the ratio between the maximum width of the frontal horns relative to the maximum diameter of the skull. In addition, the use of callosal angle values to help diagnose NPH in patients who have an EI value at the pathological cut-off limit (0.30-0.34) can also be performed. Basically, the narrower the callosal angle (50-800; normal value is 100-1200), the more likely the individual is to be diagnosed with NPH. Zhou and Xia mentioned that the use of EI to diagnose NPH is very crucial, considering that although the disease can be cured, it also has the potential to not be diagnosed quickly. The same study also mentions an EI value > 0.30 as a limitation of radiological findings for diagnosing NPH if acute symptoms are not found [7,12].

In this study, there were 6 patients with an age range of 52-81 years who, based on the interpretation of the researchers and comparisons, had an EI value of >0.30. Considering that this study also conducted an analysis of the relationship between increasing EI values and age, the findings of higher values in older age groups could certainly be anticipated by researchers. Nonetheless, the clinical significance of the EI value > 0.30 in this study can be used as a basis for findings in the form of a possible diagnosis of NPH in this group of individuals, and acts as a "variation" of the participants included in this study. EI which is able to represent ventricular volume indirectly can be used as a diagnostic tool or predictor of NPH which is easy, does not require special tools, and is quickly performed. The finding of the possibility of NPH in the group of patients tested can be additional information for this study, namely the mean age of patients with EI > 0.30 was 62.7 ± 10.4 years; much higher than the average age of all participants (41.86 ± 17.49 years).

Apart from being associated with increasing age, ventricular enlargement is also associated with several neurodegenerative pathologies which of course also occur in old age. Thus, the use of EI which has a general

cut-off value of 0.30 can be used as a basis for suspecting a pathological process that occurs in the patient concerned, so that the EI value can be a predictor of chronic disease [5,8,10,13,14]. Furthermore, every clinician should always consider the patient's related examination findings such as whether there are signs and symptoms of NPH in patients with increased EI values to differentiate a pathological process or a purely degenerative process (brain atrophy and ventriculomegaly). As part of atrophy, ventriculomegaly itself is part of the compensation due to decreased brain volume, resulting in relative dilation of the ventricles to the intracranial space which causes an increase in the EI value [15].

Additional analysis of the relationship between education level and EI value did not show statistically significant results (P > 0.05) even though participants with an bachelor education level had the highest average EI value based on quantitative-descriptive analysis (0.27 ± 0.02). Other studies that have discussed the correlation between EI values and education levels have also not been found by researchers. Del Brutto et al. states that there is an inverse correlation between the two variables, which means that the higher the EI value of an individual, the lower the MoCA (Montreal Cognitive Assessment) test score will be found, indicating that the individual has cognitive impairment [16]. Basically, a person's cognitive value is not necessarily directly related to the level of education even though the indirect relationship can be understood in general. However, until now the researchers stated that there was no relationship between education level and EI scores as reported in this study.

Research Limitation

Some limitations that may have a prominent role or even act as a differentiator compared to existing studies lie in the details of the reported analysis. For example, several studies such as Arun et al., also conducted a descriptive analysis of the widest Anterior Horn Width (AHW) and Inner Diameter of the Skull (IDS) values, which are basically part of the EI calculation formula. Both of these were not reported in detail in this study although an in-depth analysis of age and gender groups was performed. Nevertheless, the use of EI in the assessment of intracranial structures such as the ventricles can still be justified radiologically or even clinically, given the high accuracy and fairly uniform cut-off values used in several studies around the world. Differences between the gender may still be an issue that is quite implicated in relation to EI, such as whether there are really significant differences between men and women, or there are no differences at all, or maybe the role of ethnicity and race can influence the results of EI examinations in both gender. On the other hand, EI itself is considered predictable based on age group by considering the results of this study and some of the previously mentioned literature; who concluded that there was a linear correlative relationship between age and an increase in the EI value to the cut-off value as seen in this study.

CONCLUSION

The average Evan's Index (EI) score in participants who underwent head CT scans was at a value of 0.26 ± 0.03 regardless of the independent variables studied, namely the gender and age of the participants. There is a relationship between the increase in the age group of the participants and the increase in the EI value which is linear and correlative. There was no difference in EI values between gender and level of formal education regardless of the age group of the individuals analyzed.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

FUNDING

This research has received no external funding.

COMPETING INTERESTS

None.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

ACKNOWLEDGMENTS

None

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