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EXAMINING THE RELATIONSHIP BETWEEN LATERAL VENTRICLE VOLUMETRIC INDEX AND LINEAR INDEXES IN CHILDHOOD AND ADOLESCENCE: A RETROSPECTIVE MRI STUDY

ÇOCUKLUK VE ERGENLİKTE LATERAL VENTRİKÜL HACİMSEL İNDEKSİNİN DOĞRUSAL İNDEKSLER İLE İLİŞKİSİNİN İNCELENMESİ: RETROSPEKTİF MRG ÇALIŞMASI

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ABSTRACT

Objective: Indexes obtained from two-dimensional and three-dimensional measurements are used to evaluate the brain's lateral ventricle (LV) structure. However, there were limited studies on how well the Evans index (EI) and the Bicaudate index (BI), which estimate LV volume, represent the LV volumetric index (LVVI) in the childhood and adolescence period. This study investigated the relationship between LVVI and linear indexes (EI and BI) in the pediatric period regarding age and sex factors.

Method: This study was performed retrospectively in 588 individuals (267 [45.4%] females) aged 1-18 years with normal brain magnetic resonance images (MRI) between 2012 and 2021. LVVI was obtained by segmenting three-dimensional T1-weighted MRIs with volBrain1.0. LVVI was obtained by dividing the LV absolute volume by the total intracranial volume. We made linear measurements for EI and BI with the 3D Slicer. In this study, we compared the data obtained from individuals in 16 different age ranges between 1-18 years old with SPSS (ver.28).

Results: In our study, we found the mean value of LVVI to be 0.656±0.372%. The mean values of EI and BI were 0.242±0.025 and 0.070±0.022, respectively. In the pediatric population, we found that mean values of EI and BI were significantly higher in males than in females ($p<0.05$). In the pediatric period, LVVI had a positive correlation with EI at a moderate level (r:0.443) and with BI at a high level (r:0.624) ($p<0.001$).

Conclusion: In this study, we presented LVVI data to evaluate LV in the pediatric period. This study showed that using BI instead of EI is more effective in estimating LV volume when LVVI information is unavailable in the pediatric period.

Key Words: Lateral ventricles, Index, Three-Dimensional Imaging, Child, Adolescent

ÖZ

Amaç: Beyinde lateral ventrikül (LV) yapısının değerlendirilmesinde iki boyutlu ve üç boyutlu ölçümlerden elde edilen indekslerden yararlanılmaktadır. Ancak LV hacmini tahmin eden Evans indeksinin (Eİ) ve Bicaudate indeksin (Bİ) LV hacimsel indeksini (LVVİ) çocukluk ve ergenlik dönemlerinde ne kadar temsil ettiği ile ilgili sınırlı çalışma vardı. Bu çalışma pediatrik dönemde LVVİ ile doğrusal indeksler (Eİ ve Bİ) arasındaki ilişkiyi yaş ve cinsiyet faktörleri açısından araştırdı.

Yöntem: Bu çalışma, 2012 ile 2021 yılları arasında beyin manyetik rezonans görüntüleri (MRG) normal olan 1-18 yaş arası 588 bireyde (267 [%45,4] kadın) retrospektif olarak gerçekleştirildi. LVVİ, T1 ağırlıklı volümetrik MRG'lerin volBrain1.0 ile segmentasyonu ile elde edildi. LV hacminin total intrakranial hacme oranlanması ile LVVİ elde edildi. Eİ ve Bİ için doğrusal ölçümler 3D Slicer ile yapıldı. Bu çalışmada 1-18 yaş arası 16 farklı yaş aralığındaki bireylerin verileri SPSS (ver.28) ile karşılaştırıldı.

Bulgular: Çalışmamızda LVVİ ortalama değerini % 0.656±0.372 bulduk. Eİ ve Bİ ortalama değerleri ise sırasıyla 0.242±0.025 ve 0.070±0.022 idi. Pediatrik popülasyonda, ortalama Eİ ve Bİ değerleri erkeklerde kadınlara göre istatistiksel olarak anlamlı yüksekti ($p<0.05$). Pediatrik dönemde LVVİ, Eİ ile orta seviyede (r: 0.443), Bİ ile yüksek seviyede (r: 0.624) pozitif bir korelasyona sahipti ($p<0.001$).

Sonuç: Bu çalışma ile çocukluk ve ergenlik dönemlerinde LV'nin değerlendirilmesinde kullanılacak LVVİ verileri sunuldu. LV hacim bilgisine çeşitli nedenler ile ulaşılamaması durumunda Eİ yerine Bİ'nin kullanılmasının LV hacmini tahmin etmede daha efektif olduğu gösterildi.

Anahtar Kelimeler: Lateral ventriküller, İndeks, Üç Boyutlu Görüntüleme, Çocuk, Ergen

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INTRODUCTION

The lateral ventricle (LV) is a structure deep in both cerebral hemispheres filled with cerebrospinal fluid (CSF). The LV, limited by the anatomical structures around it, can be compared to a wide letter "C" with its opening facing forward. The upper parts of these spaces in both brain hemispheres are adjacent through the septum pellicidum. However, their lower parts are separated from each other in both temporal lobes. The LV has parts within the frontal, temporal, and occipital lobes called "horns" and a body within the parietal lobe. The triangular-shaped region at the junction of the body of the LV and the temporal horn and occipital horn is called the collateral trigone (atrium) [1].

It has been reported that the structure of the LV is affected by brain maturation, aging, and various diseases [2]. It is challenging to distinguish the pathological structure of the LV from its normal anatomy during brain maturation that continues throughout childhood and adolescence. In this process, indexes created by linear measurements from various regions of the LV were used as biomarkers. The Evans index (EI) was the most commonly used of these indices [3]. EI was calculated as the ratio of the LV's frontal horns' maximum width to the skull's maximum internal diameter on the same line in pneumoencephalograms. EI was also examined with cross-sectional images, and its diagnostic reliability was confirmed [3]. Later, the bicaudate index (BI) was proposed as an alternative to EI [4]. BI is the ratio of the width of the narrowest area between the head of caudate nuclei to the distance between the inner diameter of the skull on the same line.

Various studies have reported that three-dimensional (3D) volumetric measurements provide more sensitive and accurate results than two-dimensional (2D) linear measurements in evaluating LV pathologies [5,6]. Today, LV volume data can be easily obtained thanks to fully automatic segmentation software. However, this software utilizes specialized 3D imaging modalities for LV volume data instead of conventional MRI. For this reason, indexes obtained from 2D images, which give faster results, are still frequently used in the clinical practice. The ability of indexes obtained with 2D measurements to represent changes in 3D structure is controversial. In addition, correlation studies between volume measurement, the best method for evaluating LV, and linear indices were limited. Reinard et al. reported that the correlation and inter-rater reliability of ventricular volume and measurements made from the frontal horn of the LV were high [7]. Various studies have investigated to what extent the indexes calculated through the frontal horn region of the LV represent the ventricular volume of the LV [8–10]. Ambarki et al. [8] investigated the relationship between EI and total ventricular volume in elderly individuals, and Bourne et al. [10] investigated in adults. Ragan et al. compared the volume data of the entire ventricular system with various linear indexes in 22 hydrocephalus patients and 22 controls in the pediatric period [9]. We think that since these linear indexes are made from measurements between the frontal horn regions of the LV, it would be more accurate to compare them with the volume of the LV instead of the total ventricular volume. Therefore, unlike other studies, this study aims to investigate the relationship between LV volumetric index (LVVI) and linear indexes (EI and BI) in a large pediatric cohort. In this way, we will investigate how effective EI and BI, frequently used in clinical practice, are in predicting LV volume.

Some studies, including small numbers of pediatric individuals, had different results regarding the sexual dimorphism of EI and BI [11–15]. Studies investigating normal EI and BI values in large pediatric cohorts did not investigate sex differences [16,17]. For these reasons, the second aim of this study was to look for evidence of sexual dimorphism in EI, BI, and LVVI.

METHOD

Study Design and Participants

In this study, we took advantage of children and adolescents from different research to evaluate the association of LVVI with EI and BI during childhood and adolescence [18]. We retrospectively examined patients aged 0-18 who had MRIs between 2012 and 2021 using the radiological picture archiving and communication system (PACS). The first criterion for inclusion in this study was that patients had a 3D T1-weighted sequence in the MRI protocol to measure volumetric and linear indexes. The second criterion was that the pediatric radiologist reported that the patients had “normal radiological anatomy.” The third criterion was that pediatric individuals were not followed up with any definitive neurological or psychiatric disease diagnosis, according to radiology and hospital information system records.

We excluded pediatric patients with cerebral or cerebellar pathology who did not have normal radiological anatomy. However, the group we used for normative data included pediatric individuals who underwent MRI to rule out headache, convulsions, and epileptogenic pathology.

To determine normative data of LV indexes specific to age groups, we determined 16 different age groups between the ages of 1-18. We created six subgroups during six months of infancy and early childhood (between the ages of 1-3), the fastest period of brain development. In addition, we created five subgroups in 12-month periods between the ages of 4-8 and 5 subgroups in 24-month periods between the ages of 9-18.

Magnetic Resonance Imaging Method and Analysis

This study used the 3D-T1 weighted Fast Field Echo (FFE) MRI sequence obtained from a 3 Tesla MRI device (Achieva 3.0 T TX; Philips Medical Systems, Best, Netherlands). The voxel size of this sequence is isotropic (1 x 1 x 1 mm^3), and the slice thickness is 1 mm (FOV: 250 mm; TR: 8.2 ms; TE: 3.8 ms; FA: 80; image matrix: 240 x 240).

Linear Measurement Analysis for Evans Index and Bicaudate Index: For linear measurements, we used the 3D Slicer v.4.10.2 program (Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA). These measurements were made by a single observer (SI) with ten years of experience in medical imaging techniques. The first author (SI), an anatomist, remeasured the MRIs of three randomly selected pediatric individuals from each age group (48 individuals) to analyze intraobserver reliability. The second author (DS), a pediatric radiologist, remeasured these pediatric individuals to analyze interobserver reliability.

For each pediatric individual, we made linear measurements parallel to the anterior commissure – posterior commissure (AC-PC) plane and in the first section where the LV meets the foramen of Monro. We detected this cross-section with the help of 3D Slicer's "slice intersections" and "reformat widget" (Figure 1). We made all the linear measurements in our study with the electronic caliper of the 3D Slicer on this axial section. We found the EI by rationing the maximum width of the frontal horns of the LV to the maximum internal diameter of the skull, which we measured in the same section (Figure 1b) [3,19]. We found the BI by proportioning the width of the narrowest area between the head of caudate nuclei to the distance between the inner diameter of the skull on the same line (Figure 1b) [4]. We used Microsoft Office Excel 2016 (Microsoft Windows) to calculate the indexes

The Lateral Ventricle’s Volumetric Analysis: We obtained LVVI data from volBrain1.0, a fully automatic segmentation software [20]. volBrain1.0 is a free online platform located at https://volbrain.net/. volBrain1.0 provides LVVI information by rationing LV to total intracranial cavity volume (TIV) and does not require any installation or training [20]. This software provides LVVI information as a percentage (%).

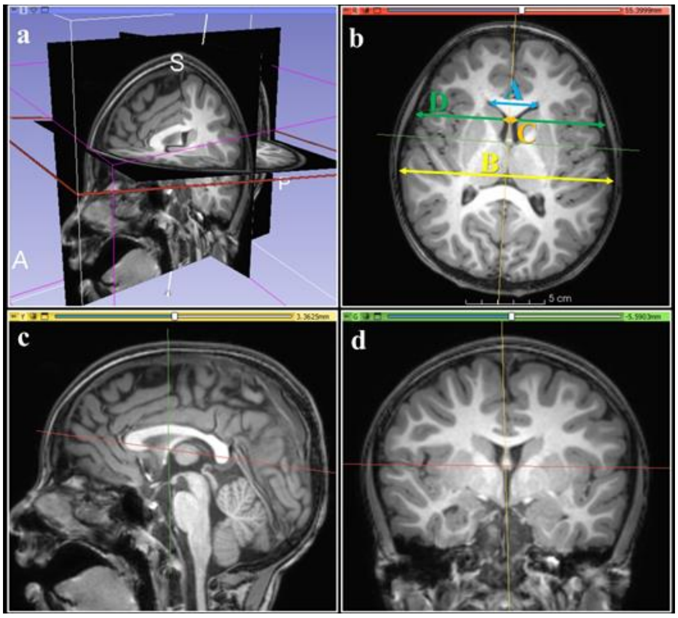

Figure 1. Determination of the axial section where linear measurements are made for Evans Index and Bicaudate Index with 3D Slicer. We detected the axial cross-section (b) with the help of 3D Slicer's "slice intersections" and "head reformat widget" (a). With the help of the mid-sagittal section (c), we ensured that the axial section was parallel to the anterior commissure - posterior commissure (AC-PC) plane. With the help of coronal section (d), we detected the first axial section where the lateral ventricle meets the interventricular foramen (Monro). Measurements made on this axial section (b); The maximum width measurement of the lateral ventricle anterior horns is demonstrated by the blue line (A). The measurement of the maximum internal diameter of the skull is demonstrated by the yellow line (B). The orange line (C) shows the measurement of the width of the narrowest area between the head regions of the caudate nucleus. The green line (D) shows the measurement of the inner diameter of the skull parallel to the measurement line between the caudate nuclei

We converted DICOM format (Digital Imaging and Communications in Medicine [.dcm]) images to NIFTI format (Neuroimaging Informatics Technology Initiative [.nii]) to obtain LVVI data using volBrain1.0. We submitted the NIFTI format files to volBrain1.0 by adding sex and age information. volBrain1.0 presented the volumetric analysis results and segmentation map (native) in the job status section. The volBrain1.0 report included several snapshots of labeling results of axial, coronal, and sagittal images of brain structures for quality control. We examined the pediatric individuals whose segmentation accuracy we doubted by uploading the native file of VolBrain1.0 to ITK Snap (ver. 3.8) software (Figure 2) [21]. We excluded those whose 2D and 3D parcellation images did not match the radiological cross-sectional images without any manual adjustments to keep the results unbiased.

Ethical Approval

The local ethics committee approved the conduct of this study (Bursa Uludag University Faculty of Medicine Clinical Research Ethics Committee, Approval Date: 19.09.2023 Decision Number: 2023-17/20). We conducted our study in accordance with the Declaration of Helsinki.

Statistical Analysis

All statistical analyzes were performed with IBM SPSS ver.28.0 (IBM SPSS Statistics for Windows, Version 28.0. [Released 2021] Armonk, NY: IBM Corp.). Our study first investigated "Is there a significant difference between the normative values of EI, BI and LVVI in 16 different periods between the ages of 1-18?" Therefore, we used One-Way Analysis of Variance (ANOVA) and Tukey Honestly Significant Difference (HSD) tests. Secondly, we examined the issue of "Is there a significant relationship between linear indexes (EI and BI) and LVVI in the pediatric period" using the Spearman rank correlation test. Thirdly, we used Student's t-test (in parametric data) or Mann-Whitney U (in non-parametric data) tests to investigate the issue of "Is there sexual dimorphism in the normative values of EI, BI, and LVVI?" Finally, we used the intraclass correlation coefficients (ICC) test to investigate the question "Is there intra-observer or inter-observer agreement in linear measurements?" In the statistical tests we used, the significance value was accepted as $p<0.05$.

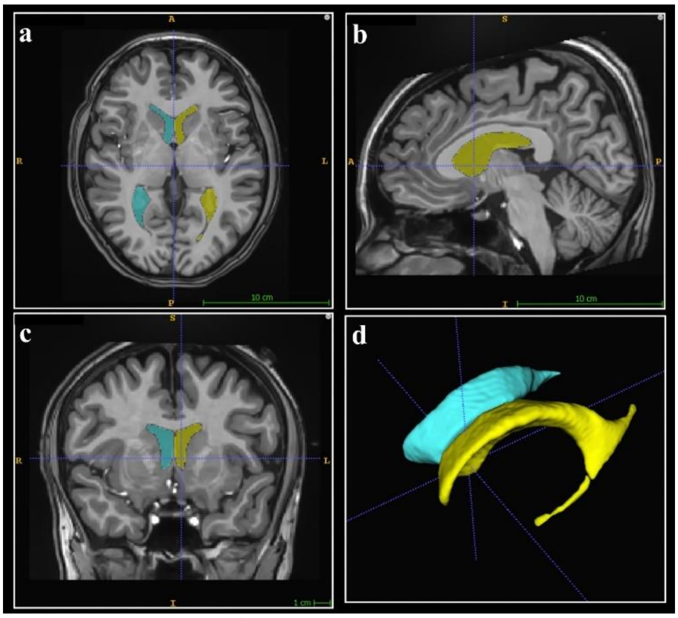

Figure 2. Examination of axial (a), sagittal (b), coronal (c), and three-dimensional (d) segmentation of the lateral ventricle using ITK Snap. The right lateral ventricle is represented in blue, and the left lateral ventricle in yellow

RESULTS

We conducted this study with 588 pediatric individuals (mean age: 6.99±5.37) who had MRIs between 2012 and 2021 and met the inclusion criteria of our research. Males participated in our study at a rate of 54.6% (321 individuals; mean age: 5.20±0.29) and females at a rate of 45.4% (267 individuals; mean age: 5.56±0.34). The quantitative status of pediatric individuals in 16 different age groups in our study according to sex was presented in Figure 3.

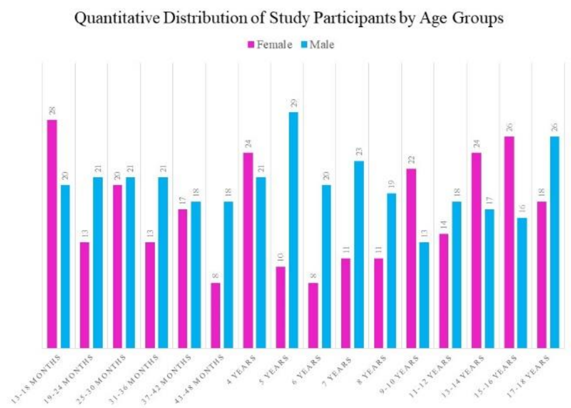

Figure 3. Quantitative distribution of pediatric individuals included in the study according to sex in 16 different age ranges

We presented the mean values of LVVI, EI, and BI data in age groups, regardless of the sex factor, in Table 1. We reported the sex comparison of index values across age groups in Table 2. In this study, we found LVVI mean values in the 1-18 age group 0.656 ± 0.372%. The mean values of EI and BI were 0.242 ± 0.025 and 0.070 ± 0.022, respectively. The highest values of all the indexes we examined were between 13-18.99 months. The lateral ventricle volumetric index had its lowest values at 7 years of age, EI at 43-48.99 months, and BI at 9-10 years of age (Table 1). We did not find a statistically significant difference between sexes in LVVI (p: 0.474; Table 2). In the pediatric population, we found that the mean values of EI and BI are significantly higher in males than females (p<0.05). In the sex comparison in the age groups, we found a significant difference in EI's 31-36.99 months, eight years, 11-12 years, and 15-16 age groups. We found that BI showed sexual dimorphism in 13-18.99 months, 5, 7, and 11-12 age groups (p<0.05; Table 2).

Table 1. Comparison of sex-independent Lateral ventricle volumetric index, Evans index, and Bicaudate index in 16 age group between 1-18 years

Age Groups	Lateral Ventricle Volumetric Index (%)		Evans Index		Bicaudate Index	
	Mean	±SD	Mean	±SD	Mean	±SD
13-18.99 m	0.794 $^{\beta}$	0.424	0.248 $^{\beta}$	0.030	0.084 $^{\beta}$	0.025
19-24.99 m	0.641	0.301	0.243	0.018	0.075	0.019
25-30.99 m	0.713	0.421	0.246	0.024	0.072	0.022
31-36.99 m	0.592	0.288	0.239	0.020	0.070	0.025
37-42.99 m	0.547	0.267	0.244	0.018	0.062	0.019
43-48.99 m	0.661	0.319	0.234*	0.030	0.072	0.018
4 y	0.597	0.248	0.244	0.022	0.068	0.018
5 y	0.607	0.332	0.245	0.020	0.067	0.019
6 y	0.669	0.396	0.248	0.024	0.071	0.025
7 y	0.538*	0.291	0.242	0.030	0.064	0.017
8 y	0.599	0.344	0.236	0.020	0.062	0.021
9-10 y	0.562	0.385	0.236	0.023	0.061*	0.018
11-12 y	0.661	0.415	0.242	0.022	0.065	0.022
13-14 y	0.741	0.468	0.243	0.027	0.071	0.021
15-16 y	0.731	0.405	0.238	0.032	0.076	0.021
17-18 y	0.739	0.431	0.245	0.023	0.077	0.022
1-18 y (Total)	0.656	0.372	0.242	0.025	0.070	0.022

m: months; y: years; Descriptive statistics were given as mean and standard deviation (SD). The highest mean values are indicated in the table with an upper sign " β," and the lowest mean values are indicated with an upper sign ""*

In the ANOVA test, we found a significant difference in other variables except EI between the ages of 1-18 (p<0.05). In the Post Hoc Tukey HSD test, only BI had two significant clusters between 13-18.99 months and other age groups (p<0.05). The correlation test did not find a significant difference between the age factor and EI, BI, and LVVI (p<0.05).

In the pediatric period, LVVI had a moderate positive correlation with EI (p<0.001; r:0.443). There was no statistically significant correlation between 37 – 42.99 months, 9-10 years, and 13-14 age groups between LVVI and EI in age groups (p>0.05). We detected positive correlations between low (r: 0.298) and high (r: 0.688) in other age groups (Table 3). LVVI had a high positive correlation with BI in the pediatric period (p<0.001; r: 0.624). In age groups, we found LVVI had a moderate-high positive correlation (p<0.001; 0.513 < r < 0.769) in all age groups with BI (except 19-24.99 months) (Table 3). Intraobserver ICCs ranged from 0.93 to 0.99, and interobserver ICCs ranged from 0.89 to 0.97.

DISCUSSION

Meese et al. examined changes in the width of the CSF spaces throughout life on CT images of 170 healthy individuals. They noted that values in the first twenty years of life differ significantly from all other ages and that separate studies should be conducted for younger age groups [22]. Bourne et al. reported that the volume index was the gold standard in the quantitative evaluation of LV [10]. Neikter et al. reported that ventricular volume was a more accurate method of evaluating changes in ventricular structure than the Evans index [6]. Therefore, our study presented LVVI data specific to age groups that can be used in the clinical evaluation of LV between the ages of 1 and 18. However, LVVI data may not be available from conventional MR images. Therefore, we examined the relationship between two linear indexes commonly used in the clinic and LVVI and found that BI had a higher correlation than EI. For this reason, we recommend using BI instead of EI in LV volume estimates using the anterior horn of the LV.

LVVI change between ages 1-18: In diagnostic radiology, visual examination of the volume and shape of the ventricles is a standard procedure [8]. Giedd et al. stated that an increased ventricular/brain volume ratio is an integral part of normal pediatric development [23]. In this study, we found that LVVI has the highest value in early childhood, decreasing until the beginning of adolescence and increasing until the age of 18. Karacan et al. found that the ratio of LV to brain volume was highest between the ages of 6-9 (1.04%) and lowest between the ages of 10-13 (0.89%). They also found an increase between the ages of 14-17 (0.98%) compared to the previous period [24]. Barron et al. reported that the relative volume of LV was lower in childhood (0-9 years: 1.8%) than in adolescence (10-19 years: 3.3%) [25]. Our study supported studies that found the absolute volume of the LV in adolescence to be higher than in childhood [24–26]. The most important reason why the LVVI values we found in this study are lower than those of other authors may be because other authors did not include individuals in early childhood and the difference in their pediatric cohorts. Additionally, the volume measurement software we used and the ratio of LV to intracranial cavity volume instead of brain volume may also impact the results.

Relationship between linear indexes and LVVI between the ages of 1-18: EI, defined in encephalography by Evans in 1942, is widely used in cross-sectional imaging methods today. Although this index has various criticisms, it helps detect ventriculomegaly due to cerebral atrophy and hydrocephalus. Evans et al. reported the mean value of this index to be 0.23±0.04 (normal range: 0.20-0.25) [19]. Sarı et al. found that EI was between 0.23 and 0.28 between 0 and 18 [16]. They reported the highest EI values in the first year of life in males and in the second year (1 year of age) in females. Wilk et al. reported mean EI values ranging from 0.247 to 0.263 (range: 0.218-0.312) in radiodiagnostically normal individuals aged 0-18 [17]. The mean values of EI (0.234 to 0.248) in this study's 1-18 age group were within the range reported by other authors [14,16,17]. Furthermore, our study agreed with Wilk et al., who reported that EI weakly decreased with age, but the changes between consecutive age groups were not statistically significant [17].

Pelicci et al. reported that the mean BI in pediatric individuals aged 0-15 years was 0.11±0.03 (range: 0.00 to 0.20) and that BI did not increase with age [27]. Wilk et al. reported that BI had mean values between 0.081 and 0.113 (range: 0.059-0.152) between 0-18 and decreased with age (r: -0.26) [17]. Kumbar et al. found that BI was 0.0958 between the ages of 1 and 10 and 0.1036 between the ages of 11 and 20. [14]. The mean BI values (0.052 - 0.076) in this study's 1-18 age group were within the range of values stated by other authors, but our mean values were lower [14,17]. The highest BI (0.0836) we found in our study was between 13-18.99 months and differed significantly from other age groups. Although this index had lower results between the ages of 2 and 14 (0.0612-0.0750) than between the ages of 15 and 18 (0.0764-0.0772), this difference did not reach statistical significance. Doraiswamy et al. found a positive correlation (r: 0.59) between the age factor and BI in adults (between 22 and 82 years old) [28]. However, our study has shown that the age factor is insignificant for BI in the pediatric period.

Table 2. Comparison of Evans index, Bicaudate index, and Lateral ventricle volumetric index between sexes in 16 age groups between 1-18 years of age

Age Groups	Evans Index					Bicaudate Index					Lateral Ventricle Volumetric Index (%)				
	Female		Male		p	Female		Male		p	Female		Male		p
	Mean	±SD	Mean	±SD		Mean	±SD	Mean	±SD		Mean	±SD	Mean	±SD	
13-18.99 m	0.242	0.034	0.257	0.021	0.081	0.076	0.024	0.095	0.021	**0.006**	0.794	0.466	0.794	0.369	1.000
19-24.99 m	0.236	0.018	0.248	0.016	0.058	0.068	0.018	0.079	0.019	0.100	0.690	0.334	0.611	0.283	0.468
25-30.99 m	0.246	0.022	0.245	0.026	0.893	0.070	0.023	0.075	0.020	0.528	0.714	0.435	0.711	0.418	0.985
31-36.99 m	0.228	0.017	0.246	0.018	**0.006**	0.061	0.018	0.076	0.028	0.082	0.591	0.319	0.592	0.275	0.988
37-42.99 m	0.242	0.018	0.246	0.019	0.456	0.060	0.020	0.063	0.018	0.619	0.497	0.268	0.595	0.265	0.285
43-48.99 m	0.238	0.016	0.232	0.035	0.700	0.064	0.014	0.076	0.019	0.133	0.680	0.322	0.653	0.326	0.845
4 y	0.247	0.023	0.241	0.020	0.339	0.068	0.016	0.067	0.019	0.865	0.609	0.246	0.583	0.257	0.731
5 y	0.244	0.024	0.245	0.019	0.914	0.055	0.017	0.071	0.019	**0.027**	0.514	0.328	0.639	0.333	0.310
6 y	0.242	0.024	0.251	0.024	0.396	0.058	0.016	0.076	0.026	0.081	0.480	0.286	0.745	0.414	0.112
7 y	0.233	0.015	0.245	0.034	0.270	0.056	0.021	0.068	0.014	**0.050**	0.478	0.237	0.567	0.315	0.416
8 y	0.226	0.016	0.243	0.020	**0.022**	0.052	0.016	0.067	0.022	0.058	0.528	0.208	0.640	0.402	0.400
9-10 y	0.238	0.016	0.231	0.032	0.399	0.059	0.017	0.065	0.019	0.350	0.520	0.252	0.633	0.549	0.408
11-12 y	0.232	0.020	0.249	0.021	**0.029**	0.056	0.015	0.073	0.024	**0.023**	0.563	0.297	0.737	0.483	0.247
13-14 y	0.245	0.029	0.241	0.025	0.625	0.071	0.023	0.071	0.019	0.985	0.847	0.569	0.591	0.204	0.085
15-16 y	0.230	0.036	0.251	0.021	**0.047**	0.074	0.021	0.080	0.022	0.438	0.749	0.454	0.701	0.320	0.714
17-18 y	0.238	0.026	0.250	0.021	0.093	0.071	0.021	0.082	0.022	0.097	0.613	0.281	0.827	0.497	0.106
1-18 y (Total)	0.239	0.025	0.246	0.024	**0.001**	0.066	0.021	0.074	0.022	**0.000**	0.644	0.378	0.666	0.367	0.474

m; months; y: years; Descriptive statistics were given as mean and standard deviation (SD). The "p" significance values indicate whether index variables differ between the sexes in 16 developmental periods between 1-18 years of age. The statistical significance level was determined as p<0.05. The "p" values of age groups with statistically significant sex differences in the index variables are shown in bold in the tab

Table 3. Results of the correlation of Evans and Bicaudate indexes with Lateral ventricle volumetric index between the ages of 1-18 in age groups

Age Groups	Evans Index		Bicaudate Index	
	r	p	r	p
13-18.99 m	0.492	**0.000**	0.567	**0.000**
19-24.99 m	0.548	**0.001**	0.228	0.194
25-30.99 m	0.449	**0.003**	0.638	**0.000**
31-36.99 m	0.541	**0.001**	0.662	**0.000**
37-42.99 m	0.294	0.087	0.581	**0.000**
43-48.99 m	0.517	**0.007**	0.597	**0.001**
4 y	0.298	**0.047**	0.659	**0.000**
5 y	0.506	**0.001**	0.677	**0.000**
6 y	0.688	**0.000**	0.769	**0.000**
7 y	0.605	**0.000**	0.600	**0.000**
8 y	0.612	**0.000**	0.747	**0.000**
9-10 y	0.312	0.068	0.595	**0.000**
11-12 y	0.335	0.061	0.559	**0.001**
13-14 y	0.243	0.125	0.513	**0.001**
15-16 y	0.356	**0.021**	0.710	**0.000**
17-18 y	0.643	**0.000**	0.703	**0.000**
1-18 y (Total)	0.443	**0.000**	0.624	**0.000**

m; months; y: years; In the Spearman rank correlation coefficient was indicated with "r". p<0.05 is defined as significant. The "p" values of the age groups statistically significant in the correlation test are shown in bold in the table

Toma et al. reported that EI showed a high correlation (r: 0.619) with the ratio of ventricular volume to intracranial volume [5]. Our study showed a moderate (r: 0.443) correlation between EI and LVVI in the 1-18 age group. We think that the reason for this difference may be that we examined the correlation of LVVI data with EI instead of the entire ventricular system in our study. Ambarki et al. reported a stronger correlation (r: 0.94) between EI and total ventricular volume in healthy elderly individuals than in our study [8]. We think this difference arises from the fact that the population in their study consisted of elderly individuals and the different volume measurement software (QBrain v2) they used.

Some authors have used BI as quantitative data in MRI scoring in various diseases [29]. However, studies on BI were mainly conducted in adults, and the relationship between BI and parenchymal brain changes was investigated [30]. Studies investigating the relationship between BI and ventricular volume in the pediatric period were rare. Ragan et al. aimed to find the linear index that best describes the disease with 22 hydrocephalus patients in the pediatric period [9]. They reported that the ratio of ventricular volume to intracranial volume had a low correlation with BI (r^2: 0.328) and EI (r^2: 279). Our study found a high correlation between LVVI and BI (r: 0.624) and a medium correlation between EI (r: 0.443). Therefore, we think that BI can give more sensitive predictions to changes in LV. We think that we reached results different from those of Ragan et al. due to changes in the materials and methods of our study. Garbade et al. reported that age-related changes in BI are the combined result of changes in brain and ventricular volume [30]. Therefore, evaluations with BI may be affected not only by changes in the ventricular but also in the caudate nucleus.

Sex Differences: In our study, the LVVI value was higher in men (0.67±0.37%) than in women (0.64±0.38%), but there was no statistical difference. In the study conducted by Karacan et al. in 90 healthy children between the ages of 6 and 17 using the stereological method, they did not detect a significant difference between the sexes (0.94% in males, 0.99% in females) in the ratio of LV to brain volume, similar to our study [24]. We think that the quantitative difference is due to the different materials and methods used in Karacan et al.'s study and the reasons we have mentioned before.

Some studies, including a small number of pediatric individuals, reported that EI did not differ between sexes [11,12]. However, various studies have found sexual dimorphism in both EI and BI [13–15]. Unlike others, our study was conducted in a large cohort that included only pediatric individuals and supported studies reporting male>female EI and BI values [13–15].

Some authors have compared EI and LV volume in the evaluation of ventricles in adults and recommended performing volumetric analyses [5,8]. However, Von Bezing et al. reported that linear measurements were more reliable than volumetric ratios in hydrocephalus patients [31]. Therefore, we examined both volumetric and linear indexes of the lateral ventricle in our study. Reinard et al. reported that EI was a reliable and reproducible method for determining ventricular dilatation, having the highest ICC among reviewers [7]. However, in our study, we found that BI represents LV volume better than EI.

Limitations

Radiological imaging, especially during childhood, is a challenging process for both the child and the parents. In addition, prospective studies requiring large numbers of participants are extremely costly and time-consuming. For these reasons, our study was conducted retrospectively. The participants of this study were a group of patients who underwent follow-up MR imaging to exclude headache, convulsions, and epileptogenic pathology. This patient population, which we used in a different study, was selected according to strict inclusion criteria [18]. These patients represented the population most likely to undergo MRI scanning during childhood and adolescence.

CONCLUSION

In our study, we reported the mean value of LVVI in 16 different age ranges between 1 and 18 years. We think that these data will help in the anatomical-pathological distinction of LV. We concluded that since there is sexual dimorphism in the mean values of EI and BI in the pediatric population, values specific to men and women should be used. We found that in the pediatric period, LVVI had a moderate positive correlation with EI and a high positive correlation with BI. For this reason, we showed that using BI instead of EI is more effective in estimating LV volume if LV volume information cannot be accessed for various reasons.

As a result, characterizing the age- and sex-related changes in LV morphology in typically developing pediatric individuals is important for neurological evaluation. Knowing the normal values of LV indexes helps to distinguish various pathologies. For these reasons, the data we present in this study will contribute to creating reference data.

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