Original Article

Simple and reproducible linear measurements to determine ventricular enlargement in adults

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Abstract

Background: Recent studies have suggested that Evan's Index (EI) is not accurate and instead endorse volumetric measurements. Our aim was to evaluate the reproducibility of linear measurements and their correlation to ventricular volume.

Methods: Using magnetic resonance (MR) images of 30 patients referred for normal pressure hydrocephalus (NPH), EI, frontal-occipital horn ratio (FOR), third ventricular width and height, frontal horn width (FHW), and callosal angle (CA) at the foramen of Monro and the posterior commissure (PC) were independently measured by residents in neurosurgery and radiology, a neurosurgeon and radiologist, and a medical student. Intraclass correlation coefficients (ICC) were calculated to establish inter-rater agreement among the reviewers. Pearson's correlation coefficients were done to assess the relationship of the linear measurements with total ventricular volume. Kappa analyses were performed to assess the degree of agreement between cutpoints determined by the ROC analysis for the linear measurements and reviewers' gestalt impression about ventricular size with volumetric abnormality.

Results: The overall inter-rater agreement among reviewers was almost perfect for EI (ICC = 0.913), FOR (ICC = 0.830), third ventricular width, FHW (ICC = 0.88), and CA at PC (ICC = 0.865), substantial for temporal horn width (ICC = 0.729) and CA at foramen of Monro (ICC = 0.779), and moderate for third ventricular height (ICC = 0.496). EI, FOR, third ventricular width, temporal horn width, and CA at PC measures correlated with total ventricular volume. There was fair-to-almost-perfect agreement of the individual reviewer's gestalt responses of abnormatility with volumetric abnormality. Gestalt responses were better for more senior raters.

Conclusion: Linear measurements are reliable and reproducible methods for determining ventricular enlargement.

Key Words: Evan's Index, normal pressure hydrocephalus, ventriculomegaly

INTRODUCTION

Normal pressure hydrocephalus (NPH) is a progressive disease that was first described by Adams *et al.* in 1965.[1] NPH is seen in the elderly and characterized by the clinical triad of gait disturbance, urinary incontinence, and dementia in the absence of papilledema and with normal cerebrospinal fluid (CSF) opening pressure on lumbar puncture.[1] Population-based studies estimate the prevalence of NPH to be approximately 0.5–1.4% in those aged over 65 with an incidence of 5.5 new patients per 100,000 people per year.[3,14] Early diagnosis of NPH is crucial as it is a potentially reversible cause of dementia. However, the diagnosis can be difficult to confirm because a multitude of other geriatric disorders may mimic the triad of symptoms associated with the disease.

Evan's index (EI) was first described by William Evans in 1942 as an indirect linear measurement of ventricular size on pneumoencephalography in pediatric patients. EI is calculated by the ratio of the maximal transverse diameter of the frontal horns to the maximum internal diameter of the cranium.[4] Current NPH guidelines require evidence of ventricular enlargement on brain imaging defined as an EI of 0.3 or greater prior to consideration of treatment with a ventriculo-peritoneal shunt.[12]

Recent studies have questioned the reliability of EI for assessment of ventricular size and, in light of modern brain imaging, have endorsed volumetric analysis of ventricular volume.[2,15] However, volumetric ventricular analysis is labor intensive, technically challenging (as it requires specialized software), not always available in every hospital (especially in rural settings and in developing nations), and not feasible for general neurosurgical practice since it is not reimbursable. We sought to determine whether simple, reliable, and reproducible linear measurements, including EI, could serve as effective alternatives to volumetric analysis for determining ventricular size.

MATERIALS AND METHODS

Our Institutional Review Board (IRB) approved the collection of data for this retrospective study (IRB #6628). A board-certified neurosurgeon and neuroradiologist developed the measurement guidelines that were used by the other raters as a guide for calculating all linear measurements in this study [Figure 1a-g].

We reviewed our database and selected 30 consecutive patients that had been referred for evaluation of possible NPH. The mean age was 77.4 years with a range from 43 to 90 and 67% were female. All subjects underwent coronal T1-weighted magnetic resonance (MR) imaging with a General Electric 1.5-T Signa system (GE Medical Systems, Milwaukee, WI) using a 3D spoiled gradient-echo sequence with TR/TI/TE = 7.6/1.7/500 ms, flip angle = 20 degrees, field of view (FOV) =200 × 200 mm^2, matrix size = 256 × 256, pixel size = 0.781 × 0.781 mm^2, slice thickness = 2.0 mm (voxel size = 0.781 × 0.781 × 2.0 mm^3),
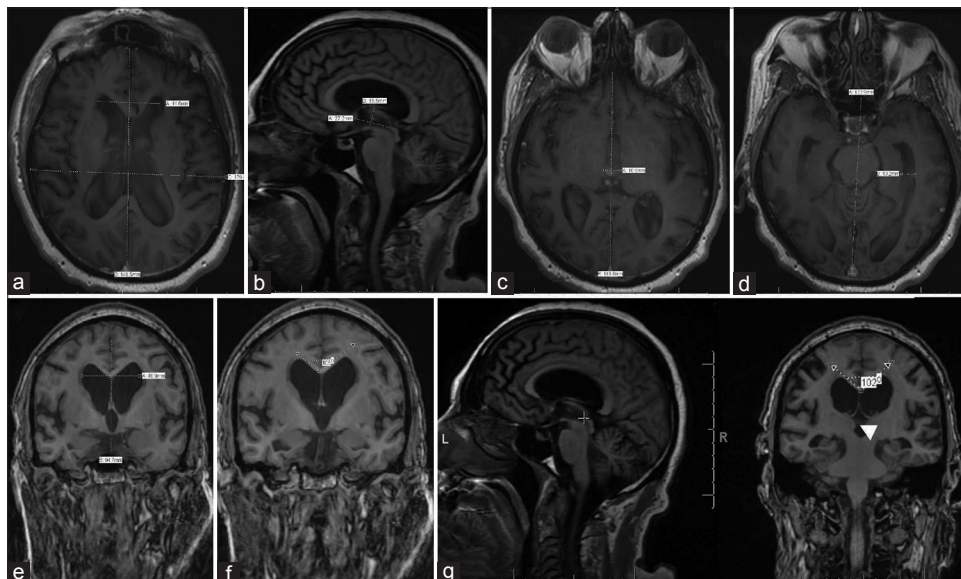

Figure 1: (a) Axial T1 MRI with the largest biparietal diameter demonstrating the midline (b) as well as the linear measurements that are perpendicular to it and parallel to one another (a, c); (b) Third ventricular height: midsagittal T1 MRI demonstrating the anterior commissure to posterior commissure (AC-PC) line (a) as well as the largest, height of the third ventricle from its floor to its roof perpendicular to the AC-PC line (b); (c) Third ventricular width: axial T1 MRI with the largest third ventricular diameter perpendicular to midline (a); (d) Temporal horn width: Axial T1 MRI with the largest temporal horn diameter perpendicular to midline (b); (e) Frontal horn width: coronal T1 MRI demonstrating largest frontal horn diameter that is perpendicular to midline (a); (f) Aial T1 MRI with the largest bifrontal distance demonstrating the callosal angle at the foramen of Monroe; (g) Coronal T1 MRI image demonstrating the callosal angle at the posterior commissure, which is confirmed by the localizer mode on the sagittal T1 image

number of slices = 124, bandwidth = 25 kHz, and scanning time of 5 min and 45 s.

Images were de-identified. They were not morphed into Talairach space. The T1-weighted (T1W) images were first converted from Digital Imaging and Communications in Medicine (DICOM) format to Analyze 7.5 format using Eigentool, an in-house software program (http://www.radiologyresearch.org/eigentool.htm). The whole brain was then segmented into 45 structures using FreeSurfer, an automated segmentation tool based on nonrigid coregistration of an atlas to the T1W MR image [Figure 2].[5] Segmentation of the brain was performed to accurately calculate the volume of ventricles and generate a gold standard. Total ventricular volume was calculated from the segmentation outcome generated by the automated software (FreeSurfer combined with preprocessing by other software tools). To improve segmentation results, before applying FreeSurfer we used a Brain Extraction Tool to eliminate nonbrain tissues in 23 patients[13] and applied field inhomogeneity correction using the N4 algorithm in Slicer (http://www.slicer.org) in 7 patients.[6,10,11,16] These tools were not included in commercial software packages and are available free of charge for research purposes. We used FreeSurfer version v. 4.5.0. Brain Extraction Tool has only one version. The segmentation results were then inspected visually. In a minority of subjects, some ventricular segmentations required manual correction by our expert because the automated segmentation did not meet the desired level of accuracy due to abnormally enlarged ventricles. Finally, the volumes of the lateral, third, and fourth ventricles were calculated from the label volumes. In all subjects, the ventricles were segmented automatically by FreeSurfer. The volumes were then calculated by multiplication of the number of voxels in each ventricle by the voxel volume. We then overlaid the segmentation outcome on the T1W image and inspected the boundaries to check the accuracy of segmentation. In 10

subjects, some parts of the segmentation outcome did not overlap with the ventricle boundary. This resulted in under-estimation of ventricle size and it required manual correction of the segmentations. Considering the large volumes of the ventricles, high resolution of the T1W images, and the clarity of ventricle boundaries, the segmentation outcomes are as accurate as gold standard.

All linear measurements were calculated independently by a medical student, a mid-level resident in neurosurgery, a neuroradiology fellow, a board-certified neurosurgeon, and a neuroradiologist. Ventricular volume was classified as normal, minimally enlarged, moderately enlarged, and grossly enlarged based on the overall impression or "gestalt" of each rater. The raters were unaware of the software calculations of intraventricular volumes.

Statistical analysis

To assess the consistency of measurements and evaluate inter-rater agreement among the reviewers, overall intraclass correlation coefficients (ICCs) were calculated for the linear measurements. Landis and Koch used the following cut points for interpreting the degree of agreement which range from less than 0 to 1 (i.e. <0 representing poor or no agreement, 0.01–0.20 slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and 0.81–1.00 almost perfect agreement).[8]

Pearson's correlation coefficients were calculated to assess the relationships of the total ventricular volume measurement with each of the individual linear measurements. These correlation coefficients of the linear measurements with total ventricular volume were then compared with each other using methods described by Yu and Dunn, which take into account the dependency in correlations.[18]

Receiver operating characteristic (ROC) methods were used to determine values for EI, frontal-occipital horn ratio (FOR), and frontal horn width (FHW) in the coronal plane that would maximize sensitivity and specificity for determining volumetric abnormality defined as an intraventricular volume ≥ 60 ml.[2] The agreement of volumetic abnormaltiy with these ROC determined cut-points for the three linear measurements, as well as the gestalt responses from the reviewers were assessed using kappa statistics, which measure the amount of agreement beyond chance. The gestalt responses for the reviewers were analyzed as 'normal' versus 'abnormal' with the latter designation including minimally, moderately, and grossly englarged ventricular volumes. Interpretation of agreement for the kappa statistic is the same as those given above for ICC. All testing was done at the 0.05 level. SAS version 9.4 was used for data analyses.
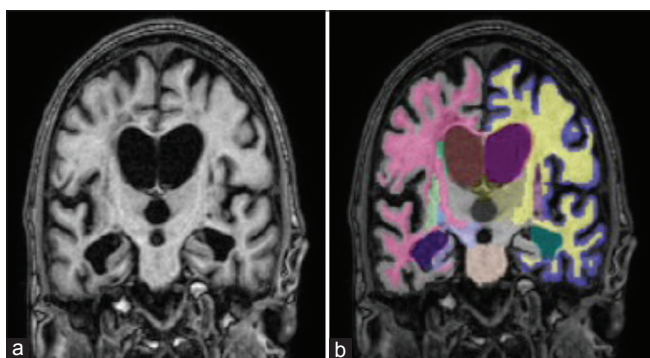

Figure 2: Segmentation of the brain using FreeSurfer in a representative T1-weighted coronal image. (a) Original image. (b) Color-coded anatomical segmentation generated by FreeSurfer overlaid on the original image

RESULTS

Overall inter-rater agreement was almost perfect for the measurements of EI, FOR, third ventricular width, FHW in coronal plane, and callosal angle (CA) at the posterior commissure (PC). Inter-rater agreement was substantial for the measurements of temporal horn width and CA at the foramen of Monro. Inter-rater agreement for third ventricular height was moderate [Table 1].

Because the inter-rater agreement was good for most of the linear measurements, the mean values for each subject were used in all subsequent analyses. The relationships between total ventricular volume and the linear measurements were significant for all measures except for third ventricular height ($P = 0.244$). EI, FOR, third ventricular width, temporal horn width, and FHW in the coronal plane were all positively associated with total ventricular volume while the CA at the foramen of Monro, and the CA at PC were negatively associated with total ventricular volume [Figure 3]. Comparison of these individual associations of the linear measurements with total ventricular volume showed that the correlations for EI, FOR, and FWH in the coronal plane were different from the other linear measurements but not from each other.

The results for the ROC analyses for the specific linear measurements identified cutpoints of 0.3 for EI, 0.42 for FOR, and 39 mm for FHW on coronal section. The kappa results for agreement with volumetric abnormality (>60 ml) along with sensitivity and specificity are given in Table 2 for these three measurements. In addition, four of the reviewers provided gestalt responses, defined as normal vs abnormal. The degree of agreement with volumetric abnormality varied across the reviewers [Table 3]. The more experienced staff had substantial to almost perfect agreement with the volume abnormality measures, which were very similar to those using the cutpoints for ER, FOR, and FHW. The neurosurgery resident also had substantial agreement while the neuroradiology fellow had fair agreement.

DISCUSSION

Idiopathic NPH has long been described as a progressive disease of the elderly who exhibit the classic triad of clinical findings (known as Hakim's triad) of instability, urinary incontinence, and dementia with ventriculomegaly.[9] Emphasis is placed on early diagnosis and treatment because CSF shunting procuedures can lead to partial reversibility and clinical improvement of the sytmpoms in approximately 60% of patients.[7] Although the presence of ventricular enlargement alone is not sufficient to diagnose NPH, it has been considered necessary (i.e., normal or small ventricles exclude NPH).[17] Ventriculomegaly has generally been

Table 1: Overall agreement of total ventricular volume with linear measurements

Measure	ICC	Agreement
Evans index	0.913	Almost perfect
FOR	0.830	Almost perfect
3rd height	0.496	Moderate
3rd weight	0.880	Almost perfect
Temporal horn width	0.729	Substantial
Frontal horn width coronal	0.895	Almost perfect
CA for Monroe	0.779	Substantial
CA at PC	0.865	Almost perfect

ICC: Intraclass correlation coefficients, FOR: Frontal-occipital horn ratio, CA: Callosal angle, PC: Posterior commissure

Table 2: Agreement of volumetric abnormality with other methods and corresponding sensitivity and specificity

Measurement	Kappa	Sensitivity (%)	Specificity (%)
Evan's index >0.3	0.781	95	82
FOR >0.41	0.851	100	82
Frontal horn >39	0.851	100	82

FOR: Frontal-occipital horn ratio

Table 3: Degree of agreement with volumetric abnormality

Neurosurgery staff gestalt	0.856	95%	91%
Neuroradiology staff gestalt	0.772	100%	73%
Neurosurgery resident gestalt	0.702	95%	73%
Radiology resident gestalt	0.322	100%	27%

defined as an EI of ≥0.3; however, recent studies have questioned the reliability of EI and recommended more complex and resource-intensive volumetric analyses.[2,15] When William Evans first described his linear measurements, it was based on the transverse diameter of the anterior horns on the anterior-posterior projections of pneumoencephalogram films.[4] These measurements have since been applied to computed tomography and MR imaging and became a standard by which ventricular enlargement has been diagnosed in the past 30 years. Some would argue that this method is prone to wide variabality among reviewers. In addition, two-dimensional methods for quantifying ventricular enlargement (i.e. EI) have their own limiations. They only address "whether the ventricles are enlarged and are not particularly informative about the relative amount of cerebral atrophy present";[12] however, in this study, the measurements of EI, FOR, and FWH had excellent reliability and consistentcy in measurement over varying levels of expertise as well as having high correlation with total ventricular volume. It is understandable with the advent of newer image-processing technology and the introduction of more sophisticated compuations, that older linear measurements methods may be marginalized in favor of three-dimensional volumetrics. Yet, it should be taken into account that in healthcare's current
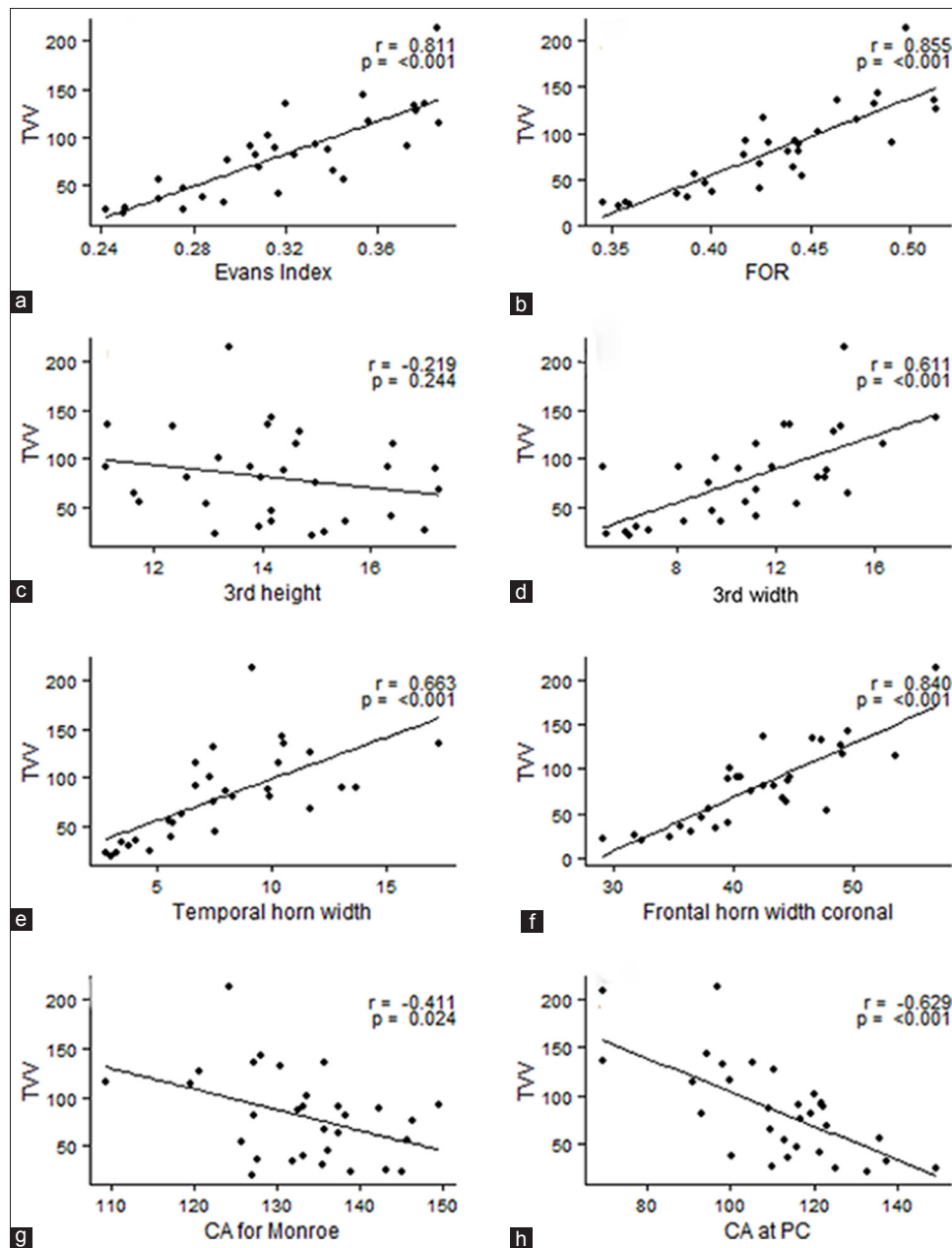
Figure 3: Correlations of the individual linear measurements with total ventricular volume (TVV). For the linear measurements, the average over all reviewers was used. (a) Evan's index; (b) Frontal-occipital Ratio; (c) Third ventricular height; (d) Thrid ventricular width; (e) Temporal horn width; (f) Frontal horn width coronal; (g) CA for Monroe; (h) CA at PC

economic climate and with ever increasing emphasis on cost-saving procedures, EI, FOR, and FHW are simple measurements that reliably determine ventricular enlargement and do not require the expensive, time-intensive and technically challenging computer software necessary for volumetric analyses. Additionally, these linear measurements may be the only modality available in some healthcare settings, such as rural areas and developing nations with no access to the latest image processing technology. One limitation of this study is the small number of subjects analysed and the small number of people analysing the data.

CONCLUSION

Current guidelines for diagnosis of NPH require evidence of ventriculomegaly, which has been historically defined by an EI of greater than 0.3. Recent studies have suggested that EI is not an accurate measure of ventricular volume and endorse volumetric measurements. Despite advances in modern brain imaging and computerized volumetric analysis, simple linear measurements such as EI continue to be fast, reimbursable, reliable, and reproducible methods for determining ventricular enlargement and feasible for general neurosurgical practice.

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