Lateral Ventricle Volume Asymmetry Predicts Midline Shift in Severe Traumatic Brain Injury

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Abstract

Midline shift following severe traumatic brain injury (sTBI) detected on computed tomography (CT) scans is an established predictor of poor outcome. We hypothesized that lateral ventricular volume (LVV) asymmetry is an earlier sign of developing asymmetric intracranial pathology than midline shift. This retrospective analysis was performed on data from 84 adults with blunt sTBI requiring a ventriculostomy who presented to a Level I trauma center. Seventy-six patients underwent serial CTs within 3 h and an average of three scans within the first 10 d of sTBI. Left and right LVVs were quantified by computer-assisted manual volumetric measurements. LVV ratios (LVR) were determined on the admission CT to evaluate ventricular asymmetry. The relationship between the admission LVR value and subsequent midline shift development was tested using receiver operating characteristic (ROC) analysis, and odds ratio (OR) and relative risk tests. Sixty patients had no >5 mm midline shift on the initial admission scan. Of these, 15 patients developed it subsequently (16 patients already had >5 mm midline shift on admission scans). For >5 mm midline shift development, admission LVR of >1.67 was shown to have a sensitivity of 73.3% and a specificity of 73.3% (area under the curve = 0.782; $p < 0.0001$). LVR of >1.67 as exposure yielded an OR of 7.56 ($p < 0.01$), and a risk ratio of 4.42 ($p < 0.01$) for midline shift development as unfavorable outcome. We propose that LVR captures LVV asymmetry and is not only related to, but also predicts the development of midline shift already at admission CT examination. Lateral ventricles may have a higher “compliance” than midline structures to developing asymmetric brain pathology. LVR analysis is simple, rapidly accomplished and may allow earlier interventions to attenuate midline shift and potentially improve ultimate outcomes.

Key words: computed tomography; midline shift; traumatic brain injury; ventricle

Introduction

TRAUMATIC BRAIN INJURY (TBI) constitutes a public health problem worldwide because of its high incidence and generally devastating consequences related to both primary and secondary injuries.^{1–3}

Prompt recognition of the extent and types of the injury is vital. Despite recent advancement in imaging methods and neural bio-

markers, computed tomography (CT) still remains the first-line tool in diagnosis, clinical management, and prognosis assessment of TBI.^{4–6} This is primarily due to its wide availability, short imaging time, high sensitivity for fractures and hemorrhage, and relatively low number of contraindications. CT scans can reveal a wide range of pathologies, of which many have been related to injury severity and outcome. Based on CT findings, numerous classifications and outcome prediction systems have been proposed^{7,8}

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with the Rotterdam⁹ and Marshall¹⁰ CT scores now most commonly and widely used.¹¹ The latter is included among clinical points in the International Mission for Prognosis and Analysis of Clinical Trials in TBI (IMPACT) prognostic calculator,^{12,13} which is one of the most established prognostic systems for TBI.

Significant (larger than 5 mm) midline shift is a CT indicator that is included in the aforementioned and several other scoring systems as a factor for poor outcome. Such asymmetric distortion and/or subfalcine herniation of the brain seems to be unfavorable, regardless of the exact underlying pathology. Asymmetric lateral ventricle compression often is associated with midline shift; however, neither its significance nor quantification have been evaluated. Only ventricle compression, irrespective of rate and sidedness, has been previously described as an indirect sign of elevated intracranial pressure.^{14,15}

In this study, we hypothesized that lateral ventricular volume (LVV) asymmetry is an earlier sign of developing asymmetric intracranial pathology than midline shift. We aimed to quantify ventricular asymmetry and evaluate its relation to subsequent midline shift development.

Methods

Subjects

This retrospective analysis was performed on data from 84 adults with blunt severe TBI (sTBI; Glasgow Coma Scale score ≤ 8) requiring a ventriculostomy presenting to a Level I trauma center (University of Florida Trauma System, Shands Hospital, Gainesville, Florida) from 2007 to 2010. For image analyses, 76 patients were included for whom both admission and follow-up CT scans were available (eight patients without follow-up imaging were excluded from the analyses). This group of patients included 57 males and 19 females, with an average age of 40 years (SD = 15.1; range, 18–75).

To test normal LVV asymmetry, a control group including 74 random patients from University of Florida Shands Hospital (26 patients) and the University of Pécs Department of Neurosurgery (48 patients) without a history of moderate or severe TBI nor any pathological CT alteration were added to the study (40 males, average age 57.27 years; SD = 18.68; range 18–93).

Approval to conduct this study was received from the institutional review boards of the University of Florida and the University of Pécs. Written informed consent was obtained from all participants (or a legally-authorized representative) in the study.

Imaging

Admission CT scans were performed within 3 h on average after injury (average = 2.44, range, 1–7; SD = 1.56 h). An average of three follow-up scans within the first 10 d of sTBI were available. Routine head trauma imaging protocol was performed on Toshiba Aquilion One helical CT scanner (Toshiba Medical Systems, Otawara, Japan). For present study, the standard, non-contrast head scans were used, acquired with the following parameters for both admission and follow-up scans: slice thickness = 5 mm, axial slices; kVp = 120; mAs = 300; field of view = 512*512 pixels (227.33 mm * 227.33 mm).

Scans of same parameters were acquired in the control group.

Image analysis

Lateral ventricle volume (LVV) measurement. Computer-assisted manual volumetric measurement was conducted using Osirix™ 5.8.5 [open source] Imaging Software (www.osirix-viewer.com).¹⁶ Left and right lateral ventricles were manually outlined (by A.T.) in each slice using the “pencil” (freehand region of interest) tool (Fig. 1). Based on the outlined areas and slice

FIG. 1. Illustration of manual lateral ventricle outlining. Left and right lateral ventricles were separately manually outlined based on image anatomy and contrast in each relevant slice. (Present image shows outlining of the left ventricle in one slice.) Then, using outlined areas from each slice and slice thickness information the software performed three-dimensional reconstruction and volume calculation of each lateral ventricle separately.

thickness information, a three dimensional (3-D) reconstruction and volume estimation of the lateral ventricle was performed. Choroid plexus and intraventricular hemorrhage were included in ventricle outlines, if present.

Inter- and intra-rater reliability of LVR measurement. Inter- and intra-rater reliability of LVR measurement was determined using Intraclass Correlation Coefficient.¹⁷ LVRs were measured on 10 random traumatic CTs twice by “rater 1” (A.T.) for intra-rater analysis, and once by “rater 2” (S.R.) for inter-rater analysis. Two-way model, absolute agreement type was applied, and both single and average measurement reliability was calculated. Analysis was run in MedCalc statistical software, version 15.4 (MedCalc Software bvba, Ostend, Belgium).¹⁸

Lateral ventricle volume ratio (LVR) calculation. Lateral ventricular asymmetry was quantified by dividing the larger LVV by the smaller, which we term the LVV ratio (LVR). For each sTBI patient’s admission scan, the LVR was calculated. Evaluators were blinded to later patient CT scans, clinical information and outcomes.

LVR also was calculated in each control patient to assess normal lateral ventricular asymmetry.

Midline shift assessment. Midline shift was measured as the distance between skull midline (line between anterior and posterior attachment of the falx to the skull) and the septum pellucidum at the level of the foramina of Monro. A midline shift greater than 5 mm

was considered significant. Midline shift was evaluated on all (admission and follow-up) scans of the sTBI patients.

Statistics

ROC analysis of LVR and midline shift development. To determine the best admission scan LVR threshold that may be associated with the development of midline shift, a receiver operating characteristic (ROC) curve analysis^{19,20} was performed using LVR as variable and midline shift development as the classification variable as follows: negative group (patients with no significant midline shift on admission or follow-up scans) and positive group (patients with no significant midline shift on admission scan but with significant midline shift present on any follow-up scans). Thus, patients with significant midline shift on admission scan were excluded from this test. ROC analysis was performed according to DeLong and colleagues²¹ (i.e., an exact binomial confidence interval for the area under the curve was calculated). ROC analysis was performed using MedCalc statistical software.¹⁸

Odds ratio and relative risk test for “high LVR” and midline shift development. The LVR threshold of best sensitivity and specificity yielded by ROC analysis (see above) was then used to define the “high admission LVR” and “low admission LVR” patient groups. Odds ratios (OR) and relative risk (RR) ratios were calculated taking the “high admission LVR” group as the exposed group; the “low admission LVR” group as the control group; patients with no midline shift on admission or follow-up scans as good outcome cases; and patients with no significant midline shift on admission scan but with significant midline shift on any follow-up scans as poor outcome cases using MedCalc statistical software.¹⁸

Results

The average LVR for all evaluated sTBI patients ($n=76$) on admission scans was 2.03 (SD=1.401); the median was 1.51 (range, 1.01 to 9.67). Sixteen patients had significant midline shift on admission scans while 60 did not. Of these 60 patients, 15 patients (25%) developed significant (>5 mm) midline shift on follow-up scans.

In the control group ($n=74$), average LVR was 1.14 (SD=0.11; median=1.11 (range, 1.00 to 1.44).

Inter- and intra-rater reliability of LVV ratio measurement

Intra-rater intraclass correlation was 0.9445 for single measures (95% confidence interval [CI]=0.8018 - 0.9858) and 0.9715 for average measures (95% CI=0.8900 - 0.9928). Inter-rater intraclass correlation was 0.9061 for single measures (95% CI=0.6840 - 0.9755) and 0.9508 for average measures (95% CI=0.8124 - 0.9876).

ROC analysis of LVR and midline shift development

Admission LVR of >1.67 was shown to have a sensitivity of 73.3% and a specificity of 73.3% for subsequent midline shift development (AUC=0.782; standard error=0.0659; 95% CI=0.657 to 0.878; z statistic=4.28; significance level p (area=0.5) <0.0001). ROC curve is shown in Figure 2.

Odds ratio and relative risk test

When using LVR of >1.67 as criterion for “high admission LVR,” 23 of 60 patients were included in the “high admission LVR” group without significant midline shift on admission scans.

FIG. 2. Receiver operating characteristic curve analysis of lateral ventricle volume ratio (LVR) on predicting subsequent midline shift development. Only patients without significant midline shift on admission scan were included. Positive group was formed by patients who developed significant midline shift on follow-up scan, negative group was formed by patients who did not.

Eleven of these patients (47.8%) developed midline shift on follow-up scans. In the “low admission LVR” group ($n=37$), four patients developed midline shift on follow-up scans (10.8%). This yielded an OR of 7.56 (95% CI=2.0173 - 28.3502; $p=0.0027$), and an RR of 4.42 (95% CI=1.5965 to 12.2586; $p=0.0042$).

Figure 3 shows a representative CT from the “high admission LVR” patient group with a LVR of 3.24 at admission (<3 h post-injury) who developed midline shift on follow-up CT scan (performed at 20 h post-injury).

Discussion

In this study, we investigated whether lateral ventricular asymmetry on admission CT scans was related to subsequent midline shift development in patients with sTBI. LVR measurement was introduced as a simple way of quantifying lateral ventricle asymmetry. In the group of patients who had no significant midline shift at admission CT scan (<3 h), ventricular asymmetry predicted subsequent midline shift development.

The best threshold of defining high lateral ventricular asymmetry was determined to be a LVR of >1.67 , which had a 73.3% sensitivity and specificity in predicting midline shift on follow-up scans (AUC=0.782). Patients with high LVR on admission scans had more than four-fold greater risk (RR=4.42) to develop subsequent significant (>5 mm) midline shift than patients with low LVR.

This value of “high” LVR (>1.67) was found to differ from the normal (control group) LVR range (the average LVR was 1.14 (SD=0.11); the median was 1.11 (range, 1.01–1.44).

It is possible that ventricles have a higher “compliance” for ongoing asymmetric pathologies and consequential inter-hemispherical pressure gradients than midline structures and therefore may

FIG. 3. Admission and follow-up computed tomography scan images of a representative patient with high admission lateral ventricle volume ratio who subsequently developed significant midline shift. Midline shift was measured 1 mm (not significant) on admission scan (<3 h post-injury; left), while it has become 7 mm (significant) on the follow-up scan at 20 h (right). The white line indicates the midline. External ventricular drainage is present on follow-up scan (hyperintense dot near right lateral ventricle).

indicate asymmetric brain pathology earlier. When unilateral hemispherical pressure is increased (e.g., by bleeding, edema), it may cause ipsilateral ventricular compression that precedes subfalcine herniation or distortion of the cerebral falx. Another possible mechanism is unilateral ventricular entrapment, where the ventricle itself causes hemispherical pressure increase and then midline shift. Figure 4 illustrates our concept of ventricular asymmetry predicting midline shift during asymmetric pathology development.

This theory also raises that compartmental pressure elevation may predict and precede general intracranial pressure increase.

No other mass effect signs may so simply and directly indicate forthcoming midline shift. It is technically difficult to evaluate other factors that would correctly indicate the level of inter-hemispheric

pressure differences such as sulcal effacement, cisternal compression, or intracranial bleeding. Moreover, these signs often appear in combination and in both hemispheres to a certain extent. Therefore, ventricular asymmetry may act as the “resultant CT sign” among other mass effect signs when evaluating inter-hemispheric pressure gradient.

Such an early indicator of asymmetric brain distortion may be clinically relevant and facilitate the detection of evolving intracranial pathology than midline shift. LVR can be quickly and reliably detected on routine CT scans using open source software. For an experienced observer, the evaluation of LVR and LVR per patient took less than 5 min to complete. This multi-slice, 3-D reconstruction of ventricles is superior to single slice or linear ventricle measurements since 3-D measurement is less affected by

FIG. 4. Concept of asymmetric intracranial pathology development. (A) 1. Normal brain. 2. Initiation of asymmetric brain pathology (e.g., bleeding, edema). 3. Pathology propagation, ipsilateral ventricle compression causing lateral ventricular asymmetry. 4. Further propagation causing midline shift. (B) 1. Normal brain. 2. Initiation of ventricular entrapment. 3. Pathology propagation, ventricle enlargement causing lateral ventricular asymmetry. 4. Further propagation causing midline shift.

image orientation and accounts for all portions (horns) of the lateral ventricles. However, in a routine clinical situation (emergency radiology) when 3D analysis may not be possible, linear measurements or subjective evaluation may still help to recognize a roughly two-fold or higher difference between lateral ventricle volumes that we propose to be predictive for midline shift. Three-dimensional analysis might be only performed in inconclusive cases.

This study has certain limitations. All patients received standard treatment for sTBI (including external ventricular drainage immediately after admission) that was modified based on the type and extent of patients' injury. Therefore, the treatment may have prevented the development of significant midline shift in some patients with lateral ventricular asymmetry on admission CT scan. Since midline shift did not necessarily develop at the time of follow-up image acquisition, it was not possible to describe the temporal features of midline shift development and compare it with lateral ventricular asymmetry dynamics.

Future studies will be needed to investigate the value of LVR as an imaging marker in outcome prediction, compared with or added to established prognostic signs and systems. However, we propose that the main benefit of recognizing a certain level of lateral ventricular asymmetry is not outcome prediction but the ability to detect the development of inter-hemispheric pressure gradient at a very early stage. Thus, categorization of patients into high- and low-risk groups for development of midline shift is possible, allowing the initiation of management strategies to attenuate midline shift.

Author Disclosure Statement

This study was funded by NIH R01 NS052831. A.T. was supported by the European Union and the State of Hungary, co-financed by the European Social Fund in the framework of TÁMOP-4.2.4.A/2-11/1-2012-0001 National Excellence Program. A.S. was funded by a grant of Hungarian Scientific Research Found OTKA- K 109132 and Bolyai Scholarship. No competing financial interests exist.

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