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ORIGINAL ARTICLE

Diagnostic accuracy of classical radiological measurements for basilar invagination of type B at MRI

José J. C. Nascimento[1] · Eulâmpio J. S. Neto[5] · Carlos F. Mello-Junior[6] · Marcelo M. Valença[1,2,3] · Severino A. Araújo-Neto[6] · Paula R. B. Diniz[1,3,4]

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Abstract

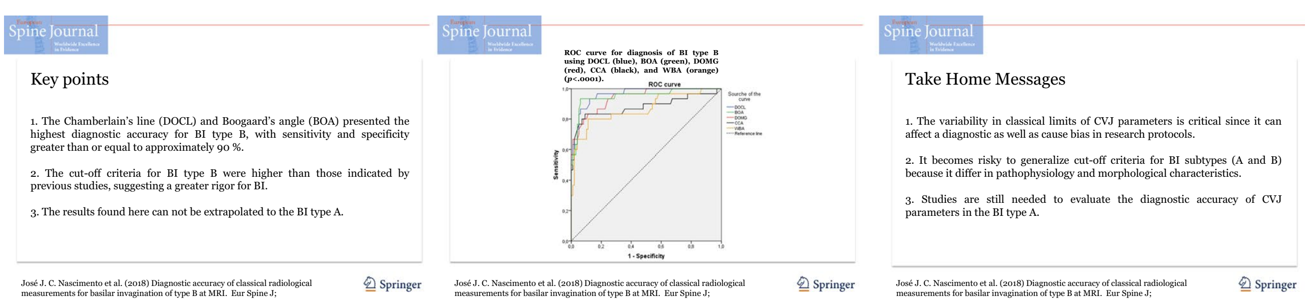
Objective To evaluate the diagnostic accuracy of classical measurements for basilar invagination (BI) of type B at MRI.

Methods This study used head MRIs from 31 participants with BI type B and 96 controls. The radiological criterion for BI was the odontoid process invagination using the obex as reference. It based on the independent prospective reading of two neuroradiologists. Concordance between the two neuroradiologists was analysed through the KAPPA index, and the discrepancy was resolved in a consensus meeting. A third examiner measured in two occasions (double blind) the distance of the odontoid apex to Chamberlain's line (DOCL) and McGregor's line (DOMG), clivus canal angle (CCA), Welcker's basal angle (WBA), and Boogaard's angle (BOA). Intra-examiner reproducibility of the measurements was evaluated with the intraclass correlation coefficient and the diagnostic accuracy by ROC curve. All analyses were at 95% confidence interval.

Results Agreement between the two neuroradiologists was statistically relevant (KAPPA = .91; $P = .0001$). The intra-examiner reproducibilities were .98 (DOCL), .97 (DOMG), .96 (CCA), .94 (WBA), and .95 (BOA) ($P < .05$). The areas under the ROC curve were .963 (DOCL), .940 (DOMG), .880 (CCA), .867 (WBA), and .951 (BOA) ($P < .05$). The cut-off criteria were ≥ 7 mm (DOCL), ≥ 8 mm (DOMG), ≤ 145° (CCA), ≥ 142° (WBA), and ≥ 136° (BOA). The diagnostic accuracies were .904 (DOCL), .870 (DOMG), .844 (CCA), .810 (WBA), and .899 (BOA).

Conclusion The DOCL and BOA presented the highest diagnostic accuracy for BI type B.

Graphical abstract These slides can be retrieved under Electronic Supplementary Material.



Keywords Basilar invagination · Chamberlain line · Boogaard's angle · Diagnostic accuracy · Roc curve

Abbreviations

BI	Basilar invagination
CVJ	Craniovertebral junction
DOCL	Apex distance of the odontoid to Chamberlain's line
DOMG	Apex distance of the odontoid to McGregor's line
CCA	Clivus canal angle

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✉ José J. C. Nascimento
josejailson64@gmail.com

Extended author information available on the last page of the article

WBA Welcker's basal angle
BOA Boogaard's angle

Introduction

Basilar invagination (BI) is an abnormality at the craniovertebral junction (CVJ) characterized by a superior projection of the odontoid process to the skull base [1]. It can be classified as type A and type B. In type A, there is an atlantoaxial luxation and the odontoid process is dislocated cephalically, for example, due to rheumatoid arthritis [2]. Clinical manifestations are relatively acute due to the direct compression of brainstem [2, 3]. Type B (or basilar impression) is related to a bone dysgenesis at the CVJ in which the skull base protrudes cephalically along with C1 and C2 as a block [2, 3]. Symptoms are longstanding and progressive affecting mainly the adult patients [4].

Generally, one or more anatomical dimorphisms are present in the BI type B. Common associated findings are platybasia, clivus hypoplasia, and occipital condyle hypoplasia [5, 6]. The clivus, which is usually vertical, may be directed horizontally so that there is a greater inclination of the foramen magnum with an apparent decrease in the volume of the posterior cranial fossa [5, 6]. It may be associated with Klippel–Feil syndrome, achondroplasia, and osteogenesis imperfect [6, 7]. Chiari malformation type I and syringomyelia are relatively frequent, and hydrocephalus may also occur [8–10].

In early studies, radiography was the only imaging method used to evaluate the CVJ morphology [11–13]. Currently, computed tomography and magnetic resonance imaging (MRI) are more suitable methods [14–16]. Several radiological measurements have been described to evaluate BI. Some of them evaluate the position of the odontoid: the distance of the odontoid process apex to Chamberlain's line (DOCL) [11] and McGregors' line (DOMG) [12], McRae's line, Wackenheim's line, and clivus canal angle (CCA) [14]. The odontoid process apex is dislocated above of all these lines in the BI type A; however, in the BI type B only the Chamberlain's and McGregor's parameters are altered [3]. Welcker's basal angle (WBA) and Boogaard's angle (BOA) are measures that represent the skull base evaluation [14, 15].

Besides their usefulness in clinical practice, classical measurements were also applied to carry out several research protocols. There are a variety of examples, such as to assess Chiari malformation [17, 18], genetic factors related to the CVJ malformations [19, 20], symptoms related to the brainstem compression [21], and post-surgical prognosis [22]. Despite published studies, data about the accuracy of these parameters in diagnosis of BI are still pending and the normality range is still variable. The aim of this study was to evaluate the diagnostic accuracy of DOCL, DOMG, CCA, WBA, and BOA for BI type B at MRI.

Methods

Study design and ethical considerations

This is a retrospective observational study addressing diagnostic test accuracy. Study design was based on Standards for Reporting Diagnostic Accuracy Studies [23]. The research protocol was approved by the institutional ethics committee, register number 65892417.3.0000.8069, being exempt from informed consent.

Participants

This study used head MRI from a radiology outpatient service. Initially, a random sampling retrieved 92 exams realized from September 2011 to November 2012. None of them had the diagnosis of BI or CVJ anomalies according to their retrospective examination reports. A second sampling phase was done to include patients with BI. This was done by a straightforward electronic search for the terms "basilar invagination" OR "basilar impression" written in head MRI reports stored in the local radiological information system (RIS) of the same imaging service. This search retrieved 39 adult patients with head MRIs performed from November 2012 to May 2017. No patient with BI had atlantoaxial luxation/instability associated (BI type A). From the first sample ($n=92$), one patient was excluded for image degradation by artefacts. From the second sample ($n=39$), three patients were excluded, one for image artefact degradation and two who had undergone prior CVJ surgery. After exclusions, both samples were mixed together, resulting in 127 head MRIs. Subsequently, all MRI exams were reviewed by two neuroradiologists (double blind) with more than 15 years of practice and blinded for sample selection and clinical data. The final criterion for BI was the odontoid process invagination using the obex as anatomical reference [24, 25] (Fig. 1). The neuroradiologists used the Osirix® (V.3.9.2) for this evaluation, and divergent readings were solved in consensus meeting.

Diagnostic tests

A third examiner blinded for clinical diagnosis and group selection calculated the CVJ measures in two occasions (double blind) separated by an interval of 4 months. The tests represented the evaluation of the odontoid process (DOCL, DOMG, and CCA) (Fig. 2) and skull base (WBA and BOA) (Fig. 3), which was done at the sagittal slice that best demonstrated the odontoid apex and other reference

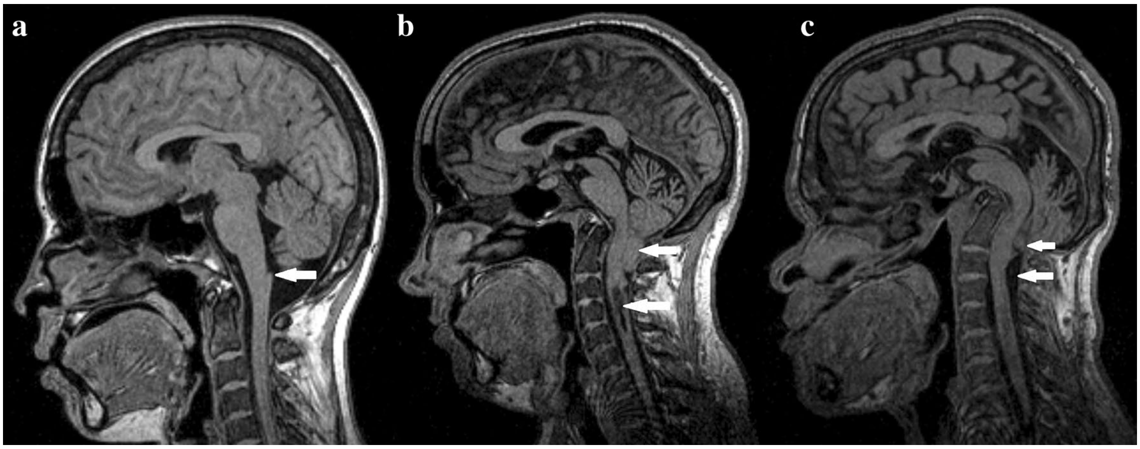


Fig. 1 Mid-MRI (T1 MR-RAGE). **a** 22-year-old female without BI showing odontoid process below obex level (arrow). DOCL: 0 mm; DOMG: 1.7 mm; CCA: 158°; WBA: 122°; BOA: 118°. **b** 31-year-old male showing BI associated with Chiari malformation (superior arrow) and syringomyelia (inferior arrow). Clinical presentation of ataxia. DOCL: 14.1 mm; DOMG: 16.2 mm; CCA: 124.6°.mm; WBA: 144.6°; BOA: 152.2°. **c** 44-year-old male showing BI associated with Chiari malformation (superior arrow) and increased CSF space (inferior arrow). Clinical presentation of converging strabismus. There is evident compression of the pons and cerebellum. Of important note is the absence of atlantoaxial luxation despite the intensity of odontoid cephalic protrusion, as in all other patients with BI type B. DOCL: 28.2 mm; DOMG: 30 mm; CCA: 101.8°; WBA: 168.6°; BOA: 189.4°

landmarks of the CVJ parameters [11, 12, 14, 15]. The measurements were performed using the Osirix® (V.3.9.2).

Exam technique

Head MRI exams were performed in a .35 T open-field Magnetom C! (Siemens Medical Solutions, Erlangen, Germany). The present study used only the non-contrast sagittal volumetric isotropic T1 (magnetization-prepared rapid gradient-echo), which is part of the protocol of that service.

Imaging parameters were as follows: slice thickness: .9–1.1 mm; FOV: 270 mm; FOV phase: 81.3%; base resolution: 256; phase and slice resolution: 100%; number of acquisitions: 1; TE: 6.5 s; TR: 18 s; and flip angle: 30°. Signal to noise ratio was adjusted by extending time acquisition up to 7–8 min, to get as close as possible of that quality acquired in high-field magnets. The whole sequence package (160 sagittal images for each patient) was available in DICOM format.

Statistical analysis

Kolmogorov–Smirnov test with Lilliefors adjustment evaluated the Gaussian distribution of the CVJ measures, and Student's t test compared them between groups. Concordance between neuroradiologists was assessed by Kappa test. Reproducibility intra-examiner for measures was analysed by the intraclass correlation coefficient. The area under the ROC curve [26] indicated the diagnostic performance of the measurements. The cut-off criterion for each test was the one that simultaneously represented the highest sensitivity and specificity [27]. Thus, accuracy represented the proportion of accurate diagnoses (positive and negative) according to their respective cut-off criteria [28]. All tests were calculated at 95% confidence interval using SPSS, version 20.

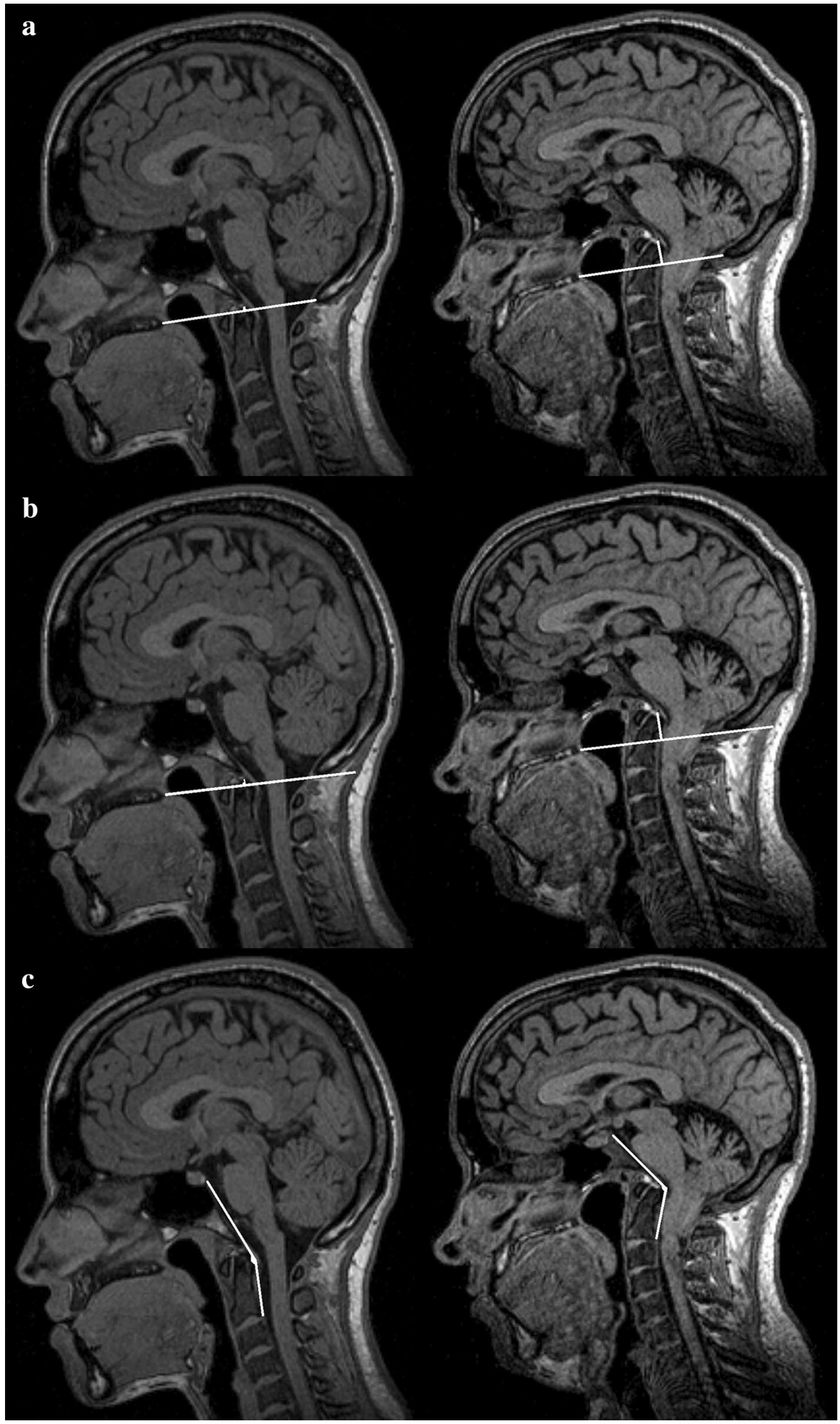
Results

Sample characteristics

Concordance between the two neuroradiologists was statistically significant (Kappa = .91; $P = .0001$). Five patients from the initial group with BI had the odontoid process below the obex and without compression of spinal cord, being classified as participant controls. Thus, 31 patients with BI type B (male = 16) and 96 controls (male = 43) represented the final sample, with a mean age of 53.9 ± 18.5 and 46.2 ± 18.6 years, respectively. The groups had no significant difference for age or gender ($P > .05$). Characterization of the groups by CVJ measurements is shown in Table 1.

In the BI group, the clinical presentations were dizziness (26%), headache (14%), neck pain (6%), seizures (18%), and motor and/or sensitive disturbances (36%). Furthermore, patients with BI presented Chiari malformation (60%), syringomyelia (30%) platybasia (80%), clivus hypoplasia (48%), and occipital condylar hypoplasia (70%), some of them in the same individual. Main reported reasons for requiring MRI in controls were epilepsy (22%), headache (23%), dementia (14%), vertigo (16%), stroke (13%), migraine disorders (4%), and hearing loss with or without tinnitus (8%).

Fig. 2 Mid-sagittal (T1 MP-RAGE) showing measures for the evaluation of the odontoid process in a control (Left) and patient with BI (Right). **a** The apex distance of the odontoid process to Chamberlain's line (DOCL), **b** the apex distance of the odontoid process to McGregor's line (DOMG), **c** a line tangent to the clivus and another tangent to the posterior margin of the odontoid process to form the clivus canal angle (CCA)



Diagnostic performance of the tests

The intra-observer agreements were .98 (DOCL), .97 (DOMG), .94 (WBA), .96 (CCA), and .95 (BOA) ($P = .0001$). The parameters DOCL and BOA showed the largest areas under the ROC curve, followed by DOMG, CCA and WBA ($P < .05$) (Fig. 4). This indicates that the parameters of Chamberlain and Boogaard had the two highest diagnostic accuracies for BI type B. The cut-off criteria were DOCL ≥ 7 mm, DOMG ≥ 8 mm, CCA ≤ 145°,

Fig. 3 Mid-sagittal (T1 MP-RAGE) showing measures for the evaluation of the skull base in a control (Left) and patient with BI (Right). **a** Welcker's basal angle (WBA) formed by two lines: one that is drawn between the nasion and the sphenoidal tubercle (angle vertex) and another from this to the anterior margin of the foramen magnum. **b** Boogaard's angle (BOA) formed by a line tangent to the clivus and another tangent to the foramen magnum

Table 1 Characterization of the groups according to the radiological measurements

Control group		Group of patients with BI type B	
Tests	Mean ± SD	Mean ± SD	*t* test
DOCL	1.8 ± 3.4	12.2 ± 5.5	*P* < .0001
DOMG	3.8 ± 3.5	13.9 ± 6.5	*P* < .0001
CCA	157 ± 9.2°	134 ± 16.4°	*P* < .0001
WBA	131.2 ± 6.7°	145 ± 10.4°	*P* < .0001
BOA	125.4 ± 6.6°	150 ± 14.4°	*P* < .0001

SD Standard deviation, *DOCL* apex distance of the odontoid process to Chamberlain's line (mm), *DOMG* apex distance of the odontoid process to McGregor's line, *CCA* clivus canal angle (°), Welcker's basal angle (°), *BOA* Boogaard's angle

WBA ≥ 142° and BOA ≥ 136°. Diagnostic accuracies were .904 (DOCL), .870 (DOMG), .844 (CCA), .810 (WBA), and .899 (BOA) (Table 2).

Discussion

Although there is clinical relevance of radiological craniometry for the evaluation and quantification of BI, the literature shows limited data about the diagnostic accuracy of the classical measurements and the limits of normality are divergent among studies. The situation is still more critical considering that the BI is classified into two types (A and B) [2, 3], that is, it becomes risky to generalize cut-off criteria for BI subtypes because it differs in pathophysiology and morphological characteristics. The present study evaluated by MRI the diagnostic accuracy of classical measurements for BI type B. Among all the classical parameters evaluated, the results showed that the DOCL had the highest diagnostic accuracy for this abnormality, and for which there was an increase in the cut-off criteria of all parameters in comparison with classical data from the literature.

Early studies [14, 15] have reported that values of DOCL are highly variable in the literature, ranging from 1 mm ± 3.6 to 6.6 mm in healthy individuals. The choice

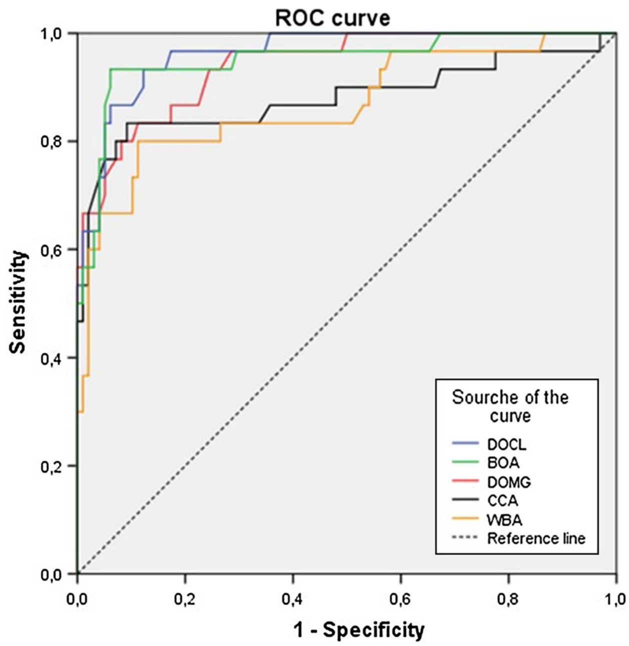


Fig. 4 ROC curve for diagnosis of BI type B using DOCL (blue), BOA (green), DOMG (red), CCA (black), and WBA (orange) ($P < .0001$)

of the cut-off criteria appears to be arbitrary within the descriptive ranges that the literature shows, which may lead to changes in the prevalence of BI in a population, or even influence the results of studies. In the present study, the results showed that the DOCL had the highest accuracy for BI type B using a cut-off criterion of 7 mm (above Chamberlain's line). This suggests that there was greater rigor for BI when compared to the limits of normality described in early studies [12, 16, 29–35]. It is important to note that many classic studies did not have MRI available, which made it difficult to evaluate the relationship between BI and brainstem, as done by authors using the obex. The DOMG, which is a variation of the DOCL, also had an increase of its cut-off criterion compared to previous data [12, 14]; however, its diagnostic performance was lower than DOCL and BOA. Thus, DOCL should be the measure of choice for evaluating BI because it has a greater diagnostic power.

The parameter CCA is another classical measure that allows measuring the posterior projection of the odontoid process in the BI [21, 22]. Studies reported that this angle can vary from 150° to 180° degrees in the flexion and extension of the head, respectively [14, 15, 36]. The CCA had the cut-off criterion of 145° in the present study. However, it is important to note that during the MRI exam the patients had their heads in the neutral position, which is part of the protocol of that service. That is, probably a patient with BI may have a greater posterior projection of the odontoid apex during daily activities that require flexion of the head, which can cause more compression of brainstem. Thus, the BI of type B must be seriously considered when a CCA is less than or equal to 145°. In the evaluation of the odontoid process, the CCA presented the lowest diagnostic performance, but this angle had greater specificity in relation to the DOMG. The CCA probably performs better in the atlantoaxial luxation (BI type A) because there is a more posterior projection in these cases.

Considering the skull base evaluation, the literature refers that the BOA has a normal variation of 119°–135° [37], being more obtuse in cases of BI type B. The results here showed that using a cut-off criterion of 136° the BOA had the second best diagnostic performance. This was not surprising because this measure uses the clivus and foramen magnum as anatomic landmarks, places where the pathophysiology of BI type B occurs [5]. Thus, the BOA should be considered in cases of BI type B together with DOCL, or an alternative parameter of the DOCL for that those cases where Chamberlain's line is difficult to calculate. In turn, the literature reports that the WBA has the mean value of 132° in individuals without CVJ abnormalities and that values greater than 140° (platybasia) are frequently associated with BI [8, 11, 14, 15]. Using the cut-off criterion of 142°, the WBA showed a good diagnostic performance; however, it had the least accuracy when compared to the other tests of this study protocol.

The present study has several limitations. First, it is desirable that the diagnostic accuracy of a test can be

Table 2 Diagnostic performance of CVJ measurements for BI type B

Tests	AUC	*P* value	Lower bound	Upper bound	Cut-off	Sensitivity	Specificity	Accuracy
DOCL	.963	< .0001	.931	.994	7 mm	.910	.900	.904
DOMG	.940	< .0001	.895	.985	8 mm	.833	.888	.870
CCA	.880	< .0001	.787	.972	145°	.800	.898	.844
WBA	.867	< .0001	.781	.952	142°	.799	.816	.810
BOA	.951	< .0001	.902	1.000	136°	.906	.910	.899

AUC area under the ROC curve, *DOCL* apex distance of the odontoid process to Chamberlain's line, *DOMG* apex distance of the odontoid process to McGregor's line, *BOA* Boogaard's angle, *WBA* Welcker's basal angle, *CCA* clivus canal angle better assessed by a quantitative reference standard, to avoid subjective interpretation biases. However, this evaluation cannot be satisfactorily done with any other craniometric parameter that has not been consistently tested for accuracy before. Therefore, the final radiological criterion for BI was the odontoid apex invagination using the obex as reference by the interpretation of two neuroradiologists. This was explored to try to represent cut-off criteria related directly to the brainstem, and consequently to the clinical importance of BI. This reflected in the cut-off criteria indicated by ROC curve, which were higher than those indicated by previous papers. Second, the control group had several clinical manifestations; the ideal would be the presence of asymptomatic patients. However, the CVJ of the control patients may be representative of a normal population because it presented measurements according to the mean ranges verified in the literature studies [14, 15, 29–32]. In addition, the CVJ measurements and morphological changes present in the group with BI reinforce him as diseased, since they are in accordance with the common findings of this pathology [5, 6, 11, 14, 15]. Third, clinical data were based on retrospective examination reports. In further diagnostic accuracy studies, patients should have also their clinical neurological data, including a detailed physical examination, prospectively collected, since many clinical manifestations of BI are non-specific and it may not be suspected at all in the first medical evaluation. Fourth, the results of the present study cannot be extrapolated to BI type A, which has a distinct pathophysiology in comparison with BI type B [38, 39]. Therefore, studies are still needed to evaluate the diagnostic accuracy of CVJ measurements in the BI type A.

The variability in classical limits of CVJ parameters is critical since it can affect the diagnosis as well as cause bias in research protocols. The absence of consensus may be related to the methodological heterogeneity of studies, as for example, standardization of sampling criteria. In addition, for diagnosis and screening of a disease it is important that the cut-off criterion should be determined, preferably, considering concepts of diagnostic performance, as for example, sensitivity, specificity, and accuracy [23], not only with descriptive statistics established within a confidence interval. The results presented here may help the practice of evidence-based medicine in the evaluation of BI type B.

In conclusion, the DOCL and BOA had the highest accuracy values for the diagnostic of BI type B, with sensitivity and specificity greater than or equal to approximately 90%.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee.

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Affiliations

José J. C. Nascimento[1] · Eulâmpio J. S. Neto[5] · Carlos F. Mello-Junior[6] · Marcelo M. Valença[1,2,3] · Severino A. Araújo-Neto[6] · Paula R. B. Diniz[1,3,4]

[1] Postgraduate Program in Neuropsychiatry, Federal University of Pernambuco, Av. Prof. Moraes Rego, 1235, University City, Recife, PE CEP: 50670-901, Brazil

[2] Neurology and Neurosurgery Unit, Clinics Hospital, Federal University of Pernambuco, Recife, Brazil

[3] Internal Medicine Department, Clinics Hospital, Federal University of Pernambuco, Recife, Brazil

[4] Telehealth Unit, Clinics Hospital, Federal University of Pernambuco, Recife, Brazil

[5] Department of Morphology, Federal University of Paraíba, João Pessoa, Brazil

[6] Diagnostic imaging, Internal Medicine, Federal University of Paraíba, João Pessoa, Brazil