



Changes in Callosal Angle and Evans' Index After Placing a Lumboperitoneal Shunt in Patients with Idiopathic-Normal-Pressure Hydrocephalus

Mustafa Cemil KILINC¹, Gokmen KAHIOGULLARI¹, Ihsan DOGAN¹, Baran Can ALPERGIN¹, Macit TERZI¹, Eda Aslanbaba BAHADIR², Muhammed Arif IBIS³, Yusuf Sukru CAGLAR¹

¹Ankara University School of Medicine, Department of Neurosurgery, Ankara, Turkey

²Ankara University School of Medicine, Department of Neurology, Ankara, Turkey

³Ankara University School of Medicine, Department of Urology, Ankara, Turkey

Corresponding author: Mustafa Cemil KILINC ✉ m.ceykl@gmail.com

ABSTRACT

AIM: To evaluate changes in the Evans' index (EI) and callosal angle (CA) in patients who underwent lumboperitoneal (LP) shunting for idiopathic normal pressure hydrocephalus (INPH) and whose symptoms improved post-operatively.

MATERIAL and METHODS: We retrospectively analysed patients who were clinically and radiologically diagnosed with INPH and treated with an LP shunt between 2010 and 2020. In all patients, we performed radiological imaging with EI and CA measurements and completed clinical assessments, including Mini-Mental State Examination (MMSE) and cognitive, urinary continence, balance and 10-m walking tests, preoperatively and post-operatively (less than 1 year later). Results were compared by statistical analyses.

RESULTS: We evaluated 42 patients who received an LP shunt for INPH and had cranial magnetic resonance imaging (MRI) performed within the first 2 months after surgery. When the pre-operative and post-operative MRIs of the patients were compared, a statistically significant decrease was found in EI and CA measurements ($p < .001$, for each). A statistically significant improvement was found in clinical tests. Post-op early radiological images predicted recovery of the gait-balance function and urinary incontinence ($p < .001$) but did not predict recovery of dementia ($p = .06$).

CONCLUSION: Radiological and clinical improvements are expected after the placement of ventriculoperitoneal (VP) or LP shunts in patients with INPH. Radiological measurements after an LP shunt in patients with INPH have not been reported in the literature. In the current study, radiological measurements after LP shunt placement were evaluated for the first time in patients with INPH. Significant changes in EI and CA after LP shunt placement may indicate whether patients will benefit clinically from an LP shunt during follow-up. A significant decrease in CA and EI measurements in the early period may be a marker for whether patients with INPH will show signs of clinical improvement and benefit from an LP shunt.

KEYWORDS: Callosal angle, Evans' index, Idiopathic normal pressure hydrocephalus, Lumboperitoneal shunt

ABBREVIATIONS: **AD:** Alzheimer's disease, **INPH:** Idiopathic normal pressure hydrocephalus, **AC:** Anterior commissure, **PC:** Posterior commissure, **CA:** Callosal angle, **MMSE:** Mini-Mental State Examination, **LP:** Lumboperitoneal shunt, **EI:** Evans index, **SD:** Standard deviation, **IQR:** Interquartile range, **MRI:** Magnetic Resonance Imaging

■ INTRODUCTION

Idiopathic normal pressure hydrocephalus (INPH) is one of the preventable causes of cognitive deterioration, gait disturbance and urination disorder in the elderly (1,7). Clinical examination and radiological images are essential for the treatment of INPH (17). Surgical treatment options should be considered in patients who do not benefit from medical treatment. Both VP and LP shunts can be safely performed in INPH (2,3,5,10,15,19). Radiological markers, such as EI, CA, temporal horn prominence, periventricular signal changes and third ventricular diameter, were used to predict the effectiveness of the treatment preoperatively. They were used as well to determine radiologically the post-operative response to treatment. In some studies, CA was considered to be a determinant of the differential diagnosis of INPH and Alzheimer's disease (AD) and secondary causes of hydrocephalus (4,9,14).

Radiological measurements performed before surgery play an important role in diagnosis and treatment planning. To date, radiological measurements have been compared and evaluated only in patients who benefited from a VP shunt. Previous studies have reported radiological criteria used in selecting patients preoperatively for VP shunt insertion (4,6). In this studies, CA and EI measurements after VP shunt insertion in patients with INPH were examined. Significant changes in those calculations indicated that patients would benefit from a VP shunt in the short term.

Although the availability and advantages of an LP shunt have been reported in patients with INPH, to our best knowledge, there are no studies showing the relationship between radiological changes and clinical improvement after an LP shunt. In this study, we aimed to measure CA and EI of the patients with INPH in the early post-operative period. With this, our goal would be to determine the surgical effectiveness and any subsequent clinical improvement in the early post-operative period.

■ MATERIAL and METHODS

Patients with INPH who were operated in our institution between 2010 and 2020 were screened and patients who received normal type LP shunt were identified. Of the 82 patients considered for inclusion, 21 had pseudotumor cerebri, 9 had high CSF pressure hydrocephalus and 52 had normal-pressure hydrocephalus. A post-operative cranial MRI was not available for 10 of the 52 patients with normal-pressure hydrocephalus and they were excluded. We included 42 patients who were clinically and radiologically diagnosed with INPH, treated with an LP shunt and had a post-operative cranial MRI in the first 2 months for any reason. There were 30 men and 12 women with a mean age of 76 years (range, 62–90 years).

This study was approved by the Ankara University Ethics Committee convened under the chairmanship of Prof. Dr. Nuray Yazihan on 04.02.2021 (Approval number: I1-57-21).

Clinical assessments, consisting of the Mini-Mental State Examination (MMSE) and cognitive, urinary continence,

balance and 10-m walking tests, were performed and evaluated by the neurology and urology departments (8). All patients were followed up for at least 12 months after surgery. Clinical tests were repeated at 1-year follow-up. Pre-operative and post-operative EI and CA were measured and compared. Statistical analysis was performed to determine the relationship between radiological and clinical changes.

Clinical Investigation and Follow-up Periods

The MMSE was performed at the neuropsychiatry clinic to measure cognitive functions. The MMSE consists of 11 questions and is evaluated over 30 points: 24–30 points are considered normal, 18–23 points are considered mild dementia and 17 and below points are considered as severe dementia. Orientation, memory, attention, calculation, recall, language, motor function and perception and visual abilities were measured. Balance and 10-m walking tests were performed at the neurology clinic to assess gait function. In the 10-m walking test, the patients walked at normal walking speed between two markers at a distance of 10 m and the elapsed time was recorded. The timed get up and go test was used to assess balance and to assess a person's mobility, requiring both static and dynamic balance control. The patients first got up from the chair and walked 3 m, subsequently turning 180° and walking back to the chair, after turning 180° sits. This period was evaluated by age. Continence testing was performed at the urology department. Changes between the pre-operative and post-operative scores for these four clinical tests were analysed and correlated with changes in MRI scans.

The mean time between pre-operative evaluation and LP shunt surgery was 4 weeks. The mean time between LP shunt placement and follow-up was 5 years. The period of the first 2 months after surgery was considered short term and the 1-year and subsequent follow ups were considered long term.

Callosal Angle and Evans' Index Measurement

CA and EI measurements were preferred because they can be performed quickly without the need for a radiologist. Modified EI was used to evaluate hydrocephalus. The largest diameters of the frontal and occipital horns were added and divided by twice the biparietal diameter. CA was measured on coronal MRI at the point where the vertical line descending from the anterior commissure and posterior commissure (AC-PC) plane 90° from the posterior commissure line intersects with the lateral ventricles (Figures 1A,B; 2A-C) (20).

Magnetic Resonance Imaging Protocol

Siemens Aera Magnetom 3 tesla MR was used to obtain two-dimensional T2-weighted gradient echo sequences with the following parameters: TR, 7.8 msec; TE, 4.3 msec. In the pilot images taken during the measurement, parallel lines on the front and back of the head intersected with the line passing through the AC and PC lines.

Statistical Analysis

Data analysis was performed using the Statistical Package for Social Science (SPSS) 26.0 software program. Descriptive statistics are provided as mean, standard deviation, median

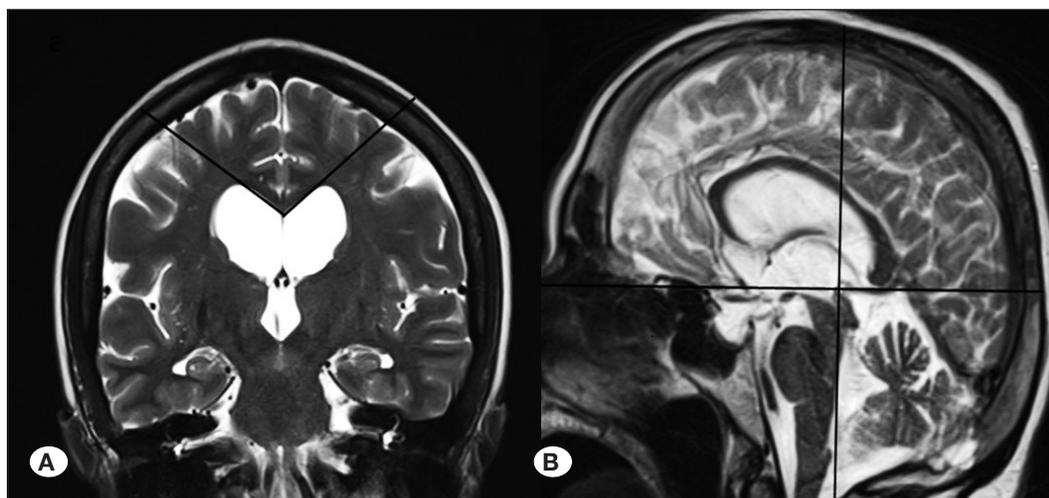


Figure 1: A) T2W coronal section callosal angle measurement. B) T2W sagittal section demonstrating the callosal angle measurement lines.

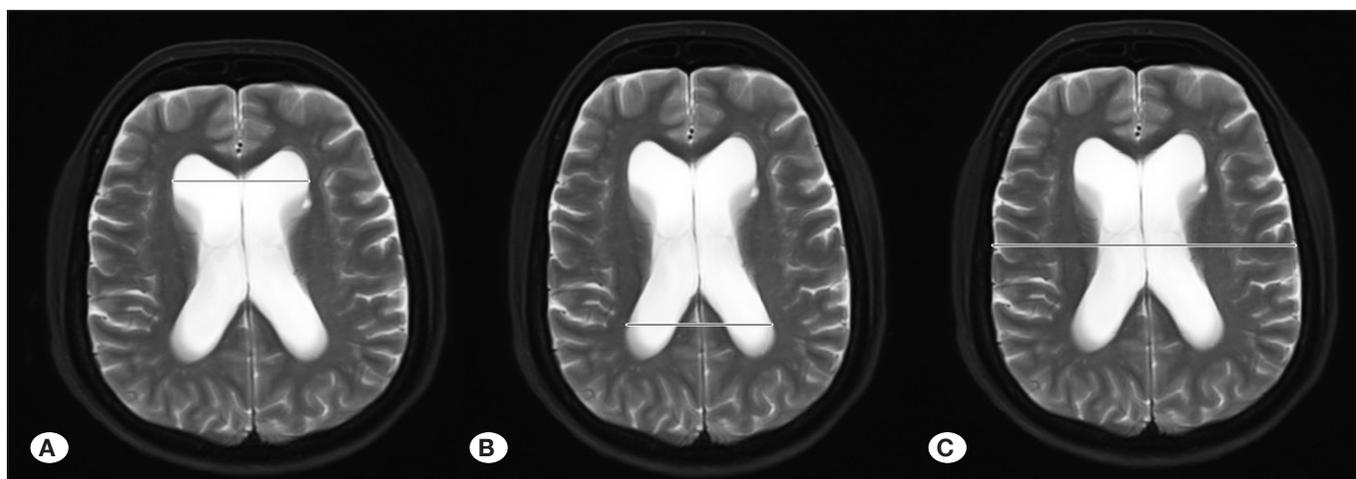


Figure 2: A) T2W axial section of the bifrontal horn diameter. B) Axial section of the bioccipital horn diameter. C) Axial section of the biparietal diameter.

and interquartile range. The suitability of numerical variables to normal distribution was evaluated using the Shapiro–Wilk test. The paired sample t-test was used to compare normally distributed variables, whereas the Wilcoxon test was used for non-normally distributed variables.

RESULTS

A revision of the distal catheter of the LP shunt was performed in 4 of the 42 patients due to abdominal swelling and shunt dysfunction. No meningitis was observed after the LP shunt. Subdural hematoma was observed in two patients after the LP shunt and recovery was achieved without any need for surgery. No complications were detected during the annual follow-up of the remaining 38 patients.

Radiological improvements were detected in 33 of 42 patients. Four of nine patients with no radiological improvements underwent shunt revision. Although five patients showed improvements in clinical possibilities, there were no radiological improvements.

The results of clinical tests along with EI and CA measurements were compared between those obtained before and after LP shunt insertion. According to the comparisons of the clinical test results, there was an average change of 1.43 points in the balance test, 1.36 points in the continence test and 2.04 points in the 10-m walking test. A statistically significant improvement was found in the gait-balance function ($p < .001$) and in urinary incontinence ($p < .001$). Although there was an average change of 0.38 points in the MMSE score after the LP shunt, no statistically significant improvement was found in dementia ($p = .06$).

When the pre-operative and post-operative MRIs of the patients were compared, there was an average change of 29.37° in the CA measurement and 0.05 points of change in the EI measurement (Figure 3A, B). A statistically significant decrease was found in EI and CA measurements ($p < .001$). Consequently, the results of the study show that patients with INPH benefited from LP shunt (Table I).

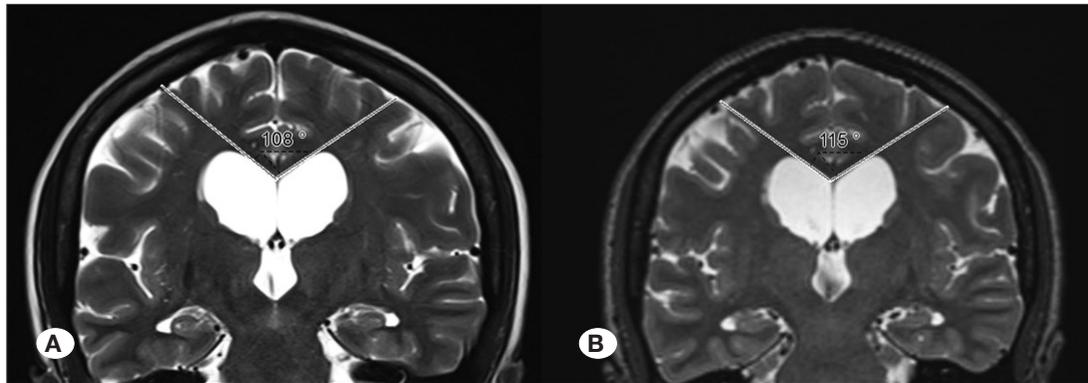


Figure 3: A) Pre-operative T2W coronal section callosal angle measurement. B) Post-operative T2W coronal section callosal angle measurement.

Table I: Statistical Analysis of Clinical Tests and Radiological Measurements

Tests		Average ± SD ¹	Median value (IQR) ²	p
MMSE Test	Pre-operative	24.00 ± 1.81	24 (3)	0.06 ^a
	Post-operative	24.38 ± 2.02	24 (3)	
Balance Test	Pre-operative	3.90 ± 1.35	4 (2)	<0.001 ^a
	Post-operative	2.47 ± 1.13	2 (1)	
Continenence Test	Pre-operative	3.45 ± 0.92	3 (1)	<0.001 ^a
	Post-operative	2.09 ± 0.90	2 (2)	
10-M Walking Test	Pre-operative	5.31 ± 1.30	5.5 (2)	<0.001 ^a
	Post-operative	3.17 ± 1.22	3 (2)	
Callosal Angle	Pre-operative	77.10 ± 7.67	76 (12.5)	<0.001 ^b
	Post-operative	106.47 ± 12.39	106.5 (16)	
Evans Index	Pre-operative	0.51 ± 0.04	0.51 (0.04)	<0.001 ^a
	Post-operative	0.46 ± 0.05	0.47 (0.07)	

¹Standard deviation (SD), ²Interquartile range (IQR), ^aPaired Samples t-test, ^bWilcoxon test. **MMSE:** Mini-mental state examination.

DISCUSSION

The severity of INPH and the outcomes of treatment with shunt insertion can be assessed with various clinical tests and radiological criteria (13). Several reported radiological markers may indicate whether or not a shunt works properly. Establishing a correlation between the clinical tests and radiological measurements that can be assessed in the short term, can help to predict the probability that a patient will benefit from the surgery in the long term. Nevertheless, no noninvasive test currently exists to show shunt functioning clearly (18).

The efficiency of radiological clinical markers such as CA and EI after shunt surgery has been reported in the literature. In those reports, these markers were shown to provide insights into whether patients with INPH would benefit from a VP shunt. Virhammar et al. reported that pre-operative CA was smaller in patients whose condition improved after shunt surgery, and measurement of CA was a useful tool in selecting shunt candidates in patients with INPH (21). Kazui et al.

reported that CA significantly predicted the response after shunt; for each degree of reduced CA, patients were 4% more likely to benefit from surgery (10). However, in some studies, radiological markers were shown not to be an indicator of shunt response. Kojoukhova et al. reported that pre-operative radiological markers were not associated with shunt response (11).

It is evident in most publications in the literature that these markers give some idea about whether patients will benefit clinically from a shunt (16). Studies conducted in patients with INPH demonstrated that CA and EI were used as pre-operative prognostic factors as well as radiological improvement indicators in post-operative follow up (20,22). The EI and CA measurements were also used for the differential diagnosis of INPH and hydrocephalus due to AD and other secondary causes. Evaluation of EI and CA measurements together provided sensitivity of 97%, specificity of 94% and accuracy of 96%, ensuring distinction between patients with INPH and AD (18).

The relationship between EI or CA measurement changes and the patient's benefit from the shunt surgery remains unclear in long-term follow-up. Whereas the clinical improvement and radiological measurements can be independent from each other, a previous study showed that radiological evaluations were strong indicators of clinical improvement in patients with INPH treated with VP shunt (13).

No studies have evaluated the pre-operative and post-operative radiological imaging and clinical assessments after an LP shunt in patients with INPH. This is the first study in which CA and EI were measured along with specific clinical tests before and after LP shunting in patients with INPH. After an LP shunt placement, maintaining walking and balance, reducing urinary incontinence and increasing cognitive functions play important roles in the clinical improvement of patients with INPH. Improvement in walking function was observed in patients in the current study after surgery. Because memory problems result from chronic degenerative processes, these problems did not improve during early follow up (12). However, during late follow-up of those patients whose hydrocephalus was seen to decrease significantly in post-operative radiological imaging, improvement in urinary incontinence problems and walking were observed. Improvements in cognitive functions were found in eight patients, but early radiological images did not predict recovery of dementia ($p=.06$).

Significant early radiological results indicated that patients would benefit from surgery during late follow up. If there are significant changes in the early period in MRI in patients with INPH who received LP shunts, the patient follow-up interval can be extended. If no significant radiological improvement is seen, strict follow-up and a repeat of the clinical tests may be required. Complication rates, such as meningitis cranial subdural hematoma, parenchymal hematoma and mechanical complications like shunt pump dysfunction, are low in LP shunts. For these reasons, an LP shunt can be safely preferred in appropriate patients with INPH.

■ CONCLUSION

In patients with INPH who underwent LP shunting, significant changes in cranial MRI seen in the early period may be the indicators of the future benefits obtained from the shunt. They can also be used to determine the frequency of follow-up.

■ AUTHORSHIP CONTRIBUTION

Study conception and design: MCK

Data collection: BCA, MT

Analysis and interpretation of results: BCA

Draft manuscript preparation: MCK

Critical revision of the article: ID, GK, YSC

Other (study supervision, fundings, materials, etc...): EAB, MAI

All authors (MCK, GK, ID, BCA, MT, EAB, MAI, YSC) reviewed the results and approved the final version of the manuscript.

■ REFERENCES

- Adams RD, Fisher CM, Hakim S, Ojemann RG, Sweet WH: Symptomatic occult hydrocephalus with "normal" cerebrospinal fluid pressure, a treatable syndrome. *N Engl J Med* 273:117-126, 1965
- Bayar MA, Tekiner A, Celik H, Yilmaz A, Menekse G, Yildirim T, Alagoz F, Guvenc F, Erdem Y: Efficacy of lumboperitoneal shunting in patients with normal-pressure hydrocephalus. *Turk Neurosurg* 28:62-66, 2018
- Bloch O, McDermott MW: Lumboperitoneal shunts for the treatment of normal-pressure hydrocephalus. *J Clin Neurosci* 19:1107-1111, 2012
- Cagnin A, Simioni M, Tagliapietra M, Citton V, Pompanin S, Della Puppa AD, Ermani R, Manara R: A simplified callosal angle measure best differentiates idiopathic-normal-pressure Hydrocephalus From neurodegenerative dementia. *J Alzheimers Dis* 46:1033-1038, 2015
- Giordan E, Palandri G, Lanzino G, Murad MH, Elder BD: Outcomes and complications of different surgical treatments for idiopathic-normal-pressure hydrocephalus: A systematic review and meta-analysis. *J Neurosurg*, 2012 (Online ahead of print)
- Grahne K, Jusue-Torres I, Szujewski C, Joyce C, Schneck M, Prabhu VC, Prabhu VC, Anderson DE: The quest for predicting sustained shunt response in normal-pressure hydrocephalus: An analysis of the callosal angle's utility. *World Neurosurg* 115: e717-e722, 2018
- Hakim S, Adams RD: The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. Observations on cerebrospinal fluid hydrodynamics. *J Neurol Sci* 2:307-327, 1965
- Hellström P, Klinge P, Tans J, Wikkelsø C: A new scale for assessment of severity and outcome in iNPH. *Acta Neurol Scand* 126:229-237, 2012
- Ishii K, Kanda T, Harada A, Miyamoto N, Kawaguchi T, Shimada K, Ohkawa S, Uemura T, Yoshikawa T, Mori E : Clinical impact of the callosal angle in the diagnosis of idiopathic-normal-pressure hydrocephalus. *Eur Radiol* 18:2678-2683, 2008
- Kazui H, Miyajima M, Mori E, Ishikawa M, SINPHONI-2 Investigators: Lumboperitoneal shunt surgery for idiopathic-normal-pressure hydrocephalus (SINPHONI-2): An open-label randomised trial. *Lancet Neurol* 14:585-594, 2015
- Kojoukhova M, Koivisto AM, Korhonen R, Remes AM, Vanninen R, Soininen H, Jääskeläinen JE, Sutela A, Leinonen V: Feasibility of radiological markers in idiopathic-normal-pressure hydrocephalus. *Acta Neurochir (Wien)* 157:1709-1718; discussion 1719, 2015
- Liu JT, Su PH: The efficacy and limitation of lumboperitoneal shunt in normal-pressure hydrocephalus. *Clin Neurol Neurosurg* 193:105748, 2020
- Meier U, Paris S, Gräwe A, Stockheim D, Hajdukova A, Mutze S: Is there a correlation between operative results and change in ventricular volume after shunt placement? A study of 60 cases of idiopathic-normal-pressure hydrocephalus. *Neuroradiology* 45:377-380, 2003

14. Miskin N, Patel H, Franceschi AM, Ades-Aron B, Le A, Damadian BE, Stanton C, Surelle Y, Golomb J, Gonen O, Rusinek H, George AE, Alzheimer's Disease Neuroimaging Initiative: Diagnosis of normal-pressure hydrocephalus: Use of traditional measures in the era of volumetric MR imaging. *Radiology* 285:197-205, 2017
15. Miyajima M, Kazui H, Mori E, Ishikawa M, on behalf of the SINPHONI-2 Investigators: One-year outcome in patients with idiopathic-normal-pressure hydrocephalus: Comparison of lumboperitoneal shunt to ventriculoperitoneal shunt. *J Neurosurg* 125:1483-1492, 2016
16. Narita W, Nishio Y, Baba T, Iizuka O, Ishihara T, Matsuda M, Iwasaki M, Tominaga T, Mori E; High-convexity tightness predicts the shunt response in idiopathic-normal-pressure hydrocephalus. *AJNR Am J Neuroradiol* 37:1831-1837, 2016
17. Relkin N, Marmarou A, Klinge P, Bergsneider M, Black PM: Diagnosing idiopathic-normal-pressure hydrocephalus. *Neurosurgery* 57:S4-16; discussion ii, 2005
18. Sakka L, Chomicki A, Gabrillargues J, Khalil T, Chazal J, Avan P: Validation of a noninvasive test routinely used in otology for the diagnosis of cerebrospinal fluid shunt malfunction in patients with normal-pressure hydrocephalus. *J Neurosurg* 124:342-349, 2016
19. Tous CT, Cutillas AMR, Infante AMJ, Granados GO, Rojas JES, Velasco B, Corral CS, Serrano MAR, Almansa AH: Adult chronic idiopathic hydrocephalus-diagnosis, treatment and evolution. *Neurocirugia (Astur)* 24:93-101, 2013
20. Virhammar J, Laurell K, Cesarini KG, Larsson EM: Increase in callosal angle and decrease in ventricular volume after shunt surgery in patients with idiopathic-normal-pressure hydrocephalus. *J Neurosurg* 130:130-135, 2018
21. Virhammar J, Laurell K, Cesarini KG, Larsson EM: The callosal angle measured on MRI as a predictor of outcome in idiopathic-normal-pressure hydrocephalus. *J Neurosurg* 120: 178-184, 2014
22. Virhammar J, Laurell K, Cesarini KG, Larsson EM: Pre-operative prognostic value of MRI findings in 108 patients with idiopathic-normal-pressure hydrocephalus. *AJNR Am J Neuroradiol* 35:2311-2318, 2014