

Results of Isotope Cisternography in 175 Patients with a Suspected Hydrocephalus

Kyeong-Seok Lee, MD¹, Sang-Mi Lee, MD², Jae-Joon Shim, MD¹,
Seok-Mann Yoon, MD¹, Hack-Gun Bae, MD¹, and Jae-Won Doh, MD¹

¹Departments of Neurosurgery, ²Nuclear Medicine, Soonchunhyang University Cheonan Hospital, Cheonan, Korea

Objective: Normal pressure hydrocephalus (NPH) is a syndrome characterized by gait disturbance, memory impairment and urinary incontinence. The isotope cisternography (ICG) became less useful because of low accuracy and complications. We tried to evaluate the safety and value of the ICG.

Methods: We retrospectively collected data on ICG of 175 consecutive patients with a suspected hydrocephalus. We classified the ICG into four types by the ventricular reflux and circulation time. The ventricular size was measured by Evans index and the width of the third ventricle.

Results: There were three complications including one case of paraplegia. Type 4 was the most common type, observed in 53%. Type 3 (33%), type 2 (7%), and type 1 (7%) were observed less often. Type 4 was more common in patients with large ventricles. Types of the ICG were not related to the causes of hydrocephalus, gender, or age of the patients. Shunting was more frequently performed in type 4 (71%), compared to type 1 (17%), type 2 (33%), and type 3 (46%). Surgery was more common when the cause was vascular. After the shunt surgery, 33.0% were graded as the improved. Although there were some improvements even in the not-improved patients, they still needed many helps. The improvement was related to the preoperative state.

Conclusion: ICG may bring a serious complication, however the incidence is very low. Although the predictability of response rate on the shunting is doubtful, ICG is a cheap and useful tool to select surgical candidates in NPH.

(Korean J Neurotrauma 2015;11(1):11-17)

KEY WORDS: Hydrocephalus · Diagnosis · Radionuclide imaging · Meningitis, aseptic · Malpractice.

Introduction

Hydrocephalus is not a single clinical entity but a complex pathophysiology with disturbed cerebrospinal fluid (CSF) circulation.²⁴⁾ Normal pressure hydrocephalus (NPH) is a syndrome that is characterized by gait disturbance, memory impairment and urinary incontinence, and is as-

sociated with ventriculomegaly in the absence of elevated CSF pressure. Diagnosis of NPH is challenging due to the absence of pathognomonic features and the broad differential for the clinical presentation.²³⁾ Various supplemental preoperative tests, including lumbar CSF tap test or CSF outflow resistance determination, were proposed to improve the accuracy of predicting a response to surgical intervention. However, the value of supplementary tests to predict which patients would benefit from placement of a shunt has not been established.²²⁾

Cisternographic studies have been in use for at least 50 years for the evaluation of abnormalities of the intracranial CSF-filled spaces.³⁾ The isotope cisternography (ICG) was previously accepted as a convenient tool to evaluate CSF dynamics,⁹⁾ even for a classification of hydrocephalus.¹²⁾ It has lost its importance in the diagnosis of NPH because of its low accuracy at predicting the outcome of shunt surgery,

Received: December 3, 2014 / **Revised:** April 7, 2015

Accepted: April 8, 2015

Address for correspondence: Kyeong-Seok Lee, MD
Department of Neurosurgery, Soonchunhyang University Cheonan Hospital, 31 Suncheonhyang 6-gil, Dongnam-gu, Cheonan 330-930, Korea

Tel: +82-41-570-3652, Fax: +82-41-572-9297

E-mail: ksleens@sch.ac.kr

© This is an Open Access article distributed under the terms of Creative Attributions Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

the radiation risk and invasiveness.^{1,19)} There were several reports on the complications after ICG, such as post-puncture headache, aseptic meningitis, and conus medullaris syndrome (CMS).^{7,14,25)} However, we still use the ICG as a useful diagnostic complement. We tried to evaluate the safety and value of the ICG in consecutive 175 patients with suspected hydrocephalus.

Materials and Methods

We retrospectively collected data on the medical records and ICG of 175 consecutive patients with a suspected hydrocephalus, which was diagnosed by computed tomography (CT) scans with or without magnetic resonance imaging

(MRI) from January 2006 to March 2013. We obtained overall 187 cisternograms, since ICG was performed twice in 12 patients. We excluded 6 patients in whom the ICG was done for the diagnosis of CSF leakage. As the complications of the ICG, we included unwanted results directly related to the ICG procedure such as subdural injections or meningitis. We excluded shunt related complications, such as shunt infections or shunt malfunctions.

We classified the findings of ICG into four types according to the ventricular reflux and circulation time; type 1 for normal migration without ventricular reflux, type 2 for delayed migration without ventricular reflux, type 3 for transient ventricular activity, and type 4 for persistent ventricular activity (Figure 1).¹³⁾ The size of the ventricles were mea-

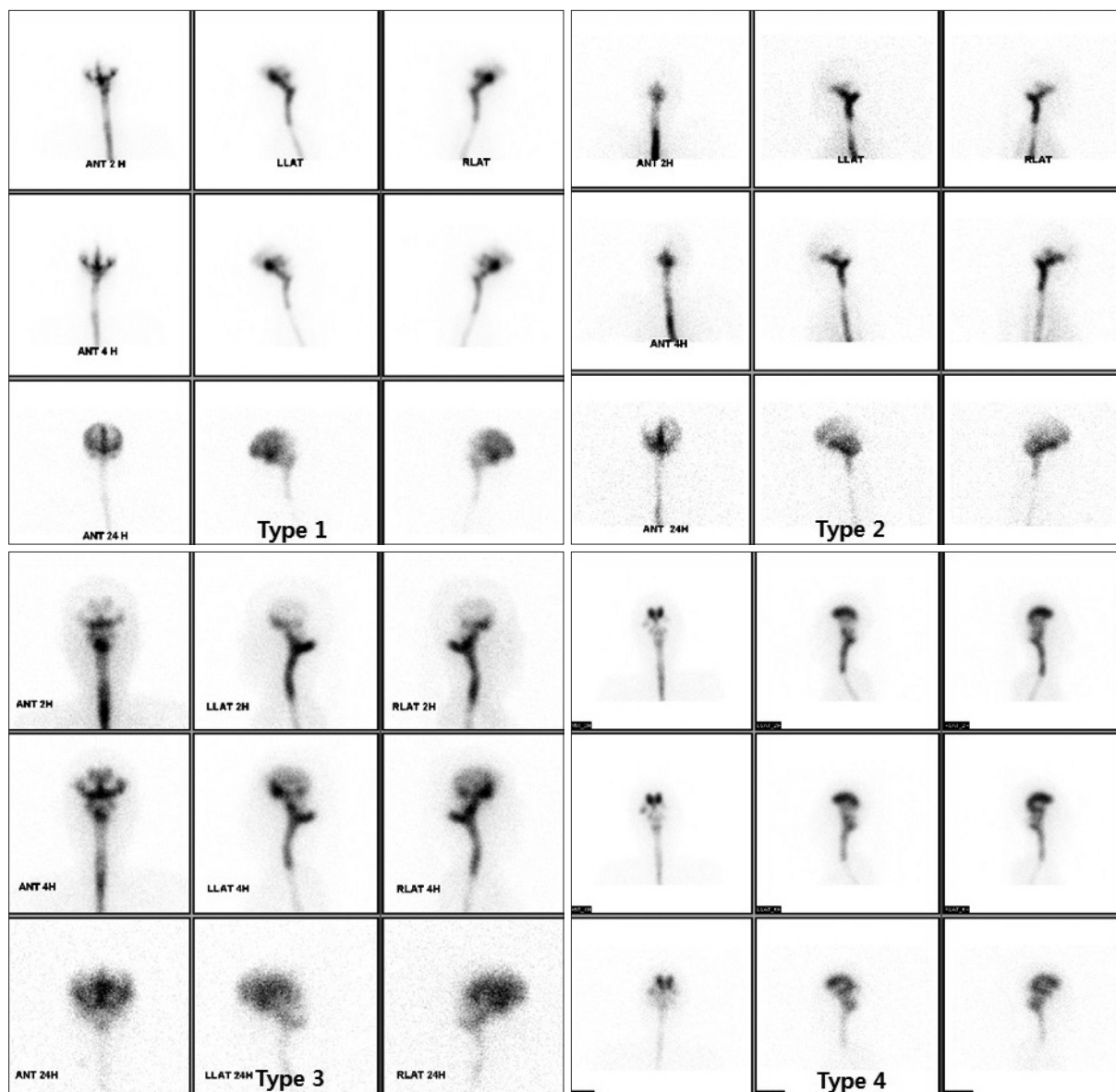


FIGURE 1. Typical findings of isotope cisternography.

sured by Evans index (EI) and the width of the third ventricle (WTV). ICG types were read by specialist of nuclear medicine.

Ventriculoperitoneal (VP) shunt was performed in 94 patients including 6 cases of revision surgery. Lumboperitoneal shunt was done in only 3 patients. Shunt surgery was performed when the symptoms of the hydrocephalus was improved after the lumbar puncture. Predicted outcome was discussed with family or relatives including failure and complications before surgery. The outcome of the shunt surgery was divided into either improved or not-improved. We evaluated the outcome and preoperative state by the Glasgow Outcome Scale (GOS). When the outcome was at least moderate disability (MD) or the patient became mobile after surgery, we graded the outcome as improved. When the outcome was severe disability (SD) or lower even after surgery, we graded the outcome as not-improved, even though there were some improvement in any symptoms.

Statistical analysis was performed using the chi-square test or Fisher's exact test. For the statistical significance, we divided the etiology into either known or unknown groups. Differences were considered significant if the *p* value was less than 0.05.

Results

There were three cases of complication including one serious complication, CMS. An 83-year-old female patient became paraplegic due to adhesive arachnoiditis, on the 4th day after ICG (type 4) without fever. Paraplegia was not recovered. There were 2 cases of subdural injection; in one patient a CT cisternography (CTC) revealed delayed clearance of contrast media without ventricular reflex (type 2), in the other patient, VP shunt revision was performed based on the previous ICG findings (type 4).

Type 4 was the most common type, observed in 92 patients (53%). Type 3 was observed in 57 patients (33%), and type 1 and 2 were observed in 12 patients (7%) in each (Table 1). Type 4 was more common in patients with high (over 3.0) EI ($p < 0.05$), or wide (over 10 mm) WTV ($p < 0.001$). Types of ICG were not related to the causes of hydrocephalus, gender, or age of the patients. Shunting was more frequently performed in type 4 (71%). The rate of shunt surgery was 17% in type 1, 17% in type 2, 46% in type 3, and 71% in type 4. This difference is statistically significant ($p < 0.0001$). Surgery was more commonly performed when the cause was vascular (Table 2). The methods of treatment were not related to the gender, WTV, or age of the patients.

TABLE 1. Clinical features of 173 patients* and results of isotope cisternography

Items	Type 1	Type 2	Type 3	Type 4	Subtotal (%)	Statistics†
Gender						$p=0.06$
Male	8	5	39	45	97 (56.1)	
Female	4	7	18	47	76 (43.9)	
Age (yr)						$p=0.52$
≤ 50	0	2	13	23	38 (22.0)	
51–70	7	7	28	46	88 (50.9)	
$71 \leq$	5	3	16	23	47 (27.2)	
Evans Index						$p < 0.05$
< 3.0	4	3	10	9	26 (15.0)	
$3.0 \leq$	8	9	47	83	147 (85.0)	
WTV (mm)						$p < 0.01$
≤ 10	4	5	20	9	38 (22.0)	
11–15	7	6	28	51	92 (53.2)	
> 15	1	1	9	32	43 (24.9)	
Causes						$p=0.31$
Trauma	6	5	24	27	62 (35.8)	
Vascular	4	4	25	54	87 (50.3)	
Idiopathic	2	1	6	8	17 (9.8)	
Others	0	2	2	3	7 (4.0)	
Treatment						$p < 0.01$
Conservative	10	8	31	27	76 (43.9)	
Surgery	2	4	26	65	97 (56.1)	
Subtotal (%)	12 (6.9)	12 (6.9)	57 (32.9)	92 (53.2)	173 (100)	

*two patients with subdural injection were excluded in this table, †type 1&2 were grouped as a single group for statistical comparison. WTV: width of third ventricle

TABLE 2. Clinical features and methods of treatment

Items	Conservative	Surgery	Subtotal (%)	Statistics
Gender				$p=0.38$
Male	46	52	98 (56.0)	
Female	31	46	77 (44.0)	
Age (yr)				$p=0.47$
≤ 50	14	24	38 (21.7)	
51–70	39	50	89 (50.9)	
$71 \leq$	24	24	48 (27.4)	
Evans Index				$p=0.051$
<3.0	16	10	26 (14.9)	
$3.0 \leq$	61	88	149 (85.1)	
WTV (mm)				$p=0.12$
≤ 10	22	17	39 (22.3)	
11–15	40	52	92 (52.6)	
>15	15	29	44 (25.1)	
Causes				$p<0.01$
Trauma	26	36	62 (35.4)	
Vascular	32	57	89 (50.9)	
Others	19	5	24 (13.7)	
Types*				$p<0.0001$
Type 1	10	2	12 (16.7)	
Type 2	8	4	12 (16.7)	
Type 3	31	26	57 (45.6)	
Type 4	27	65	92 (70.7)	
Subtotal (%)	77 (44.0)	98 (56.0)	175 (100)	

*two patients with subdural injection were excluded in numbers of cases, therefore, the subtotal numbers for types are different from other items. WTV: width of third ventricle

There was a tendency that patients with high EI underwent surgery more often, however, this difference was statistically not significant.

After the shunt surgery, 23 patients (33.0%) were graded as the improved. Although in more than a half of the not-improved patients, there were some improvements, such as improved eye opening, eye contact, or cognitive responses, they were unable to walk. They still needed helps in usual activities of daily living (ADL). Preoperatively, the GOS of the patients was MD in 11 patients, SD in 83 patients, and even vegetative state in 3 patients. The improvement rate after shunt surgery was related to the preoperative state (Table 3). Although the improvement rate of type 4 was slightly higher than that of type 3, this difference was statistically not significant.

Discussion

Many tests have been employed in the diagnosis of NPH, such as ICG, CTC, and MRI with or without intrathecal enhancement. However, there is no test that can establish a definitive diagnosis or predict shunt response.²⁾ CT or MRI

is superior to get cross-sectional images or higher spatial resolution.³⁾ However, CTC did not provide additional diagnostic value for predicting the shunt response.¹⁵⁾ Although MRI may provide useful data, it cannot always be conclusive for diagnosis and treatment planning.¹⁻³⁾ Furthermore, CT or MRI is more expensive than ICG. There are numerous dynamic test such as tap test,^{21,32)} CSF outflow resistance measures,⁵⁾ external lumbar drainage,²¹⁾ and intracranial pressure recording.^{8,27)} However, their efficacy and reliability is not fully established.²⁰⁾

There was one serious complication in 187 cisternograms (0.53%) in this series. Although ICG is generally considered to carry virtually no risk for the evaluation of NPH,²²⁾ there were some reports,^{14,20)} including four cases of CMS in 472 patients (0.85%) over the five-year period.²⁵⁾ CMS may result from a direct spinal needle injury or neurotoxicity of the radioisotope around the conus medullaris, however, the cause and mechanism of this serious complication remains unclear.²⁵⁾ Even though the safety of ICG is questionable, it is still used as a key diagnostic investigation for intracranial hypotension or CSF leakage.^{17,26,30)} Serious complications brought legal suits in Korea. A damage suit on the CMS af-

TABLE 3. Clinical features and results of shunt surgery

Items	Improved	Not improved	Subtotal (%)	Statistics
Gender				$p=0.10$
Male	13	38	51 (52.6)	
Female	19	27	46 (47.4)	
Age (yr)				$p=0.09^*$
≤ 50	4	20	24 (24.7)	
51–70	21	29	50 (51.5)	
$71 \leq$	7	16	23 (23.7)	
Evans Index				$p=0.003^*$
< 3.0	4	28	32 (33.0)	
$3.0 \leq$	28	37	65 (67.0)	
WTV (mm)				$p=0.29$
≤ 10	7	10	17 (17.5)	
11–15	19	33	52 (53.6)	
> 15	6	22	28 (28.9)	
Causes				$p=0.06^*$
Trauma	7	29	36 (37.1)	
Vascular	22	34	56 (57.7)	
Others	3	2	5 (5.2)	
Pre-Op. GOS				$p < 0.01^*$
MD	9	2	11 (11.3)	
SD, VS	23	63	86 (88.7)	
Subtotal (%)	32 (33.0)	65 (67.0)	97 (100)	

*by Fisher's test. WTV: width of third ventricle, GOS: Glasgow Outcome Scale, MD: moderate disability, SD: severe disability, VS: vegetative state

ter ICG (case number 99gahap72342) judged partial violation of liability for explanation in Korea. In another suit (case number 2002gadan67479), the local court sentenced a partial financial responsibility of the hospital, despite of the fact that the occurrence of this exceptional complication is unpredictable. ICG might become a reluctant diagnostic procedure, even though there was a sentence that there was no illegal act on the unpredictable arachnoiditis after ICG (case number 2011da100138).

Hydrocephalus is not a single clinical entity but a pathophysiological complex with various aspects.²⁴⁾ NPH may present a final common pathway for a number of different priming events.¹⁹⁾ There may be an undiagnosed co-existing structural dementia, such as Alzheimer's disease or vascular dementia.^{11,29)} Although there is an effort to make more contemporary classification schemes,²⁴⁾ there has been no consensus as to a more contemporary classification scheme, yet.²⁸⁾ Abnormal CSF dynamics are key elements of the hydrocephalus. ICG is useful to study CSF dynamics and can be a suitable diagnostic complement to help proper classification.

Shunting was more frequently performed in type 4. Type 4 was more common in patients with severe hydrocephalus;

i.e., high EI, or wide WTV. Surgery was more commonly performed when the cause was vascular. Patient selection for the shunt surgery remains challenging.¹⁰⁾ In some patients, shunting was performed based on the opinion that "they have nothing to lose,"³⁶⁾ although the chance of success was very low. The rate of shunting was not related to the gender, EI, WTV, or age of the patients.

The success rate of the shunt surgery was 33% in this study. In NPH, success rates of shunt vary from 33% to more than 90%.³¹⁾ This wide range in outcome probably reflects variations in patient selection.¹⁰⁾ Another reason of relatively poor success rate was related to the evaluating tool, the GOS. Since the majority of the patients had gait disturbance, urinary incontinence, and memory impairment, preoperative GOS of the patients was usually SD or worse. The GOS divides 5 scales including death. Even though there were some improvements, such as increased eye opening, they still needed many helps in usual ADL. The more sensitive scale may increase the improvement rate higher.¹⁸⁾ Although the GOS is too crude to evaluate the outcome of the shunt surgery, it is rather practical to reveal the actual ADL. Significant improvement was reported as approximately 29% in a review.¹⁰⁾ The improvement rate after shunt surgery was

related to the preoperative state. Early diagnosis of NPH seems to be important by the fact that hydrocephalus is the second most common potentially reversible cause of dementia and lengthy delays to diagnosis are associated with an increased rate of treatment complications and even death.⁴⁾ It has been estimated that only 10% to 20% of patients with NPH get the appropriate specialized treatment.¹⁶⁾ The early recognition of NPH before requiring a help of someone else in ADL may increase the improvement rate.

ICG was relatively safe. Although it may cause a serious complication, the incidence was quite low. To avoid complications, lumbar puncture should be placed at the lowest lumbar spinal level possible with calcium-containing diethylentriamene pentaacetate and administer no more than 1 mg.²⁵⁾ Although ICG could not accurately predict the shunt responders, it provided important information on the CSF dynamics.

Conclusion

ICG may bring a serious complication, such as paraplegia, however the incidence is very low. Although the predictability of response rate on the shunting is relatively low, ICG is a cheap and useful tool for evaluation of the hydrocephalus.

■ The authors have no financial conflicts of interest.

REFERENCES

- Algin O, Hakyemez B, Ocakoğlu G, Parlak M. MR cisternography: is it useful in the diagnosis of normal-pressure hydrocephalus and the selection of "good shunt responders"? *Diagn Interv Radiol* 17:105-111, 2011
- Algin O, Hakyemez B, Parlak M. The efficiency of PC-MRI in diagnosis of normal pressure hydrocephalus and prediction of shunt response. *Acad Radiol* 17:181-187, 2010
- Algin O, Turkbey B. Intrathecal gadolinium-enhanced MR cisternography: a comprehensive review. *AJNR Am J Neuroradiol* 34:14-22, 2013
- Ambrose T, Butler C, Myles L, Zeman A. Pitfalls in the diagnosis of hydrocephalus. *Br J Hosp Med (Lond)* 69:192-195, 2008
- Boon AJ, Tans JT, Delwel EJ, Egeler-Peerdeman SM, Hanlo PW, Wurzer HA, et al. Dutch normal-pressure hydrocephalus study: prediction of outcome after shunting by resistance to outflow of cerebrospinal fluid. *J Neurosurg* 87:687-693, 1997
- Bret P, Guyotat J, Chazal J. Is normal pressure hydrocephalus a valid concept in 2002? A reappraisal in five questions and proposal for a new designation of the syndrome as "chronic hydrocephalus". *J Neurol Neurosurg Psychiatry* 73:9-12, 2002
- Cooper JF, Harbert JC. Endotoxin as a cause of aseptic meningitis after radionuclide cisternography. *J Nucl Med* 16:809-813, 1975
- Eide PK, Brean A. Intracranial pulse pressure amplitude levels determined during preoperative assessment of subjects with possible idiopathic normal pressure hydrocephalus. *Acta Neurochir (Wien)* 148:1151-1156; discussion 1156, 2006
- Gallia GL, Rigamonti D, Williams MA. The diagnosis and treatment of idiopathic normal pressure hydrocephalus. *Nat Clin Pract Neurol* 2:375-381, 2006
- Hebb AO, Cusimano MD. Idiopathic normal pressure hydrocephalus: a systematic review of diagnosis and outcome. *Neurosurgery* 49:1166-1184; discussion 1184-1186, 2001
- Ivkovic M, Liu B, Ahmed F, Moore D, Huang C, Raj A, et al. Differential diagnosis of normal pressure hydrocephalus by MRI mean diffusivity histogram analysis. *AJNR Am J Neuroradiol* 34:1168-1174, 2013
- James AE Jr, New PF, Heinz ER, Hodges FJ, DeLand FH. A cisternographic classification of hydrocephalus. *Am J Roentgenol Radium Ther Nucl Med* 115:39-49, 1972
- Jeon BS, Myung HJ, Kim SE, Chung JK, Koh CS. Patterns of radioisotope cisternographic findings (correlation between preoperative patterns and the results of surgical shunting in patients with communicating hydrocephalus). *J Korean Neurol Assoc* 5:24-29, 1987
- Jonas S, Braunstein P. Neurogenic bladder as a complication of isotope cisternography. *J Nucl Med* 13:763-764, 1972
- Kawaguchi T, Hirata Y, Bundo M, Kondo T, Owaki H, Ito S, et al. Role of computerized tomographic cisternography in idiopathic normal pressure hydrocephalus. *Acta Neurochir (Wien)* 153:2041-2048; discussion 2048, 2011
- Kiefer M, Unterberg A. The differential diagnosis and treatment of normal-pressure hydrocephalus. *Dtsch Arztebl Int* 109:15-25; quiz 26, 2012
- Kim MK, Park BJ, Shin HS, Choi SK, Kim SB, Kim TS, et al. Clinical analysis of hydrocephalus patients who underwent shunt surgery after traumatic brain injury. *J Korean Neurosurg Soc* 7:88-91, 2011
- Klinge P, Hellström P, Tans J, Wikkelsø C; European iNPH Multicentre Study Group. One-year outcome in the European multicentre study on iNPH. *Acta Neurol Scand* 126:145-153, 2012
- Krauss JK, Halve B. Normal pressure hydrocephalus: survey on contemporary diagnostic algorithms and therapeutic decision-making in clinical practice. *Acta Neurochir (Wien)* 146:379-388; discussion 388, 2004
- Levine MC, Jayabalan V. Complications of isotope cisternography. *Ann Neurol* 1:172-176, 1977
- Malm J, Kristensen B, Karlsson T, Fagerlund M, Elfverson J, Ekstedt J. The predictive value of cerebrospinal fluid dynamic tests in patients with idiopathic adult hydrocephalus syndrome. *Arch Neurol* 52:783-789, 1995
- Marmarou A, Bergsneider M, Klinge P, Relkin N, Black PM. The value of supplemental prognostic tests for the preoperative assessment of idiopathic normal-pressure hydrocephalus. *Neurosurgery* 57(3 Suppl):S17-S28; discussion ii-v, 2005
- McGirr A, Mohammed S, Kurlan R, Cusimano MD. Clinical equipoise in idiopathic normal pressure hydrocephalus: a survey of physicians on the need for randomized controlled trials assessing the efficacy of cerebrospinal fluid diversion. *J Neurol Sci* 333:13-18, 2013
- Oi S. Classification of hydrocephalus: critical analysis of classification categories and advantages of "Multi-categorical Hydrocephalus Classification" (Mc HC). *Childs Nerv Syst* 27:1523-1533, 2011
- Park BS, Park J, Koh SH, Choi H, Yu HJ, Lee KE, et al. Conus medullaris syndrome as a complication of radioisotope cisternography. *Can J Neurol Sci* 39:347-351, 2012
- Park ES, Kim E. Spontaneous intracranial hypotension: clinical presentation, imaging features and treatment. *J Korean Neurosurg Soc* 45:1-4, 2009
- Poca MA, Mataró M, Del Mar Matarín M, Arikian F, Junqué C, Sahuquillo J. Is the placement of shunts in patients with idiopathic

- normal-pressure hydrocephalus worth the risk? Results of a study based on continuous monitoring of intracranial pressure. *J Neurosurg* 100:855-866, 2004
- 28) Rekte HL. A consensus on the classification of hydrocephalus: its utility in the assessment of abnormalities of cerebrospinal fluid dynamics. *Childs Nerv Syst* 27:1535-1541, 2011
- 29) Savolainen S, Hurskainen H, Paljärvi L, Alafuzoff I, Vapalahti M. Five-year outcome of normal pressure hydrocephalus with or without a shunt: predictive value of the clinical signs, neuropsychological evaluation and infusion test. *Acta Neurochir (Wien)* 144:515-523; discussion 523, 2002
- 30) Sehgal AK, Sethi RS, Raghavan S, Namgyal PA. Radionuclide cisternography: A prudent investigation in diagnosing spontaneous intracranial hypotension. *Indian J Nucl Med* 28:42-44, 2013
- 31) Verrees M, Selman WR. Management of normal pressure hydrocephalus. *Am Fam Physician* 70:1071-1078, 2004
- 32) Walchenbach R, Geiger E, Thomeer RT, Vanneste JA. The value of temporary external lumbar CSF drainage in predicting the outcome of shunting on normal pressure hydrocephalus. *J Neurol Neurosurg Psychiatry* 72:503-506, 2002