# Comparison Between Ventricular and Spinal Infusion Tests in Suspected Normal Pressure Hydrocephalus

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## 1 Introduction

Idiopathic normal pressure hydrocephalus (iNPH) is an often-overlooked or misdiagnosed brain disorder characterized by overt ventriculomegaly and associated with gait disturbances, cognitive impairment, and urinary incontinence. If correctly diagnosed, it is considered the only form of dementia treatable with surgery, namely through a ventriculoperitoneal or ventriculoatrial shunt with programmable valves. Despite having several diagnostic tools available, the selection of patients who will benefit from shunting still represents the main clinical challenge, as other neurological disorders can mimic iNPH or can coexist with it [1–5].

Apart from the well-known radiological signs (i.e., increased Evan's ratio, disproportionally effaced superior frontal sulci, and reduced callosal angle), functional information on perfusion, glucose metabolism, and amyloid deposit provided by positron emission tomography could be predictive of outcomes in iNPH patients, as reported in a recent review by our group [6].

Among the invasive tests to predict shunt responses, Katzman's infusion test evaluates cerebrospinal fluid (CSF) hydrodynamics [7, 8]. CSF outflow resistance (Rout) is generally regarded as the most significant parameter investigated in order to predict shunt-related neurological improvement [9]. Nonetheless, different Rout thresholds have been reported, and in 2013, a multicenter study concluded that it should not be used as a parameter to exclude patients from treatment [5].

In 2010, our group summarized 30 years of experience in the treatment of iNPH, showing that an intracranial elastance index (IEI) above 0.3 is a reliable predictor of a positive response after shunting [10]. This index is calculated by a dedicated software program developed at our institution during an intraventricular infusion test by measuring the slope of the linear regression between the diastolic intracranial pressure (ICP) values and the corresponding amplitude of each CSF pulse pressure wave.

More recently, we tried to verify the accuracy of IEI at predicting responses to shunts at both short- and long-term follow-ups in 64 patients with suspected iNPH who underwent ventricular shunting for iNPH on the basis of a positive ventricular infusion test (IEI $\geq 0.3$ and $R^2 > 0.8$) [11].

Historically, our group has performed both ventricular and lumbar infusion tests. The intraventricular infusion test (IVKT) has been considered more reliable than the Spinal Katzman Test (SKT) [5] and has allowed for obtaining deeper insights into the pathophysiology of iNPH [1].

In this study, we compare the relationship between EI and Rout in two groups (IVKT and SKT), aiming to investigate the reliability of both procedures.

## 2 Methods

Among the 856 spinal and ventricular infusion tests performed from 2001 to 2017 at our institution, we analyzed 106 cases selected for suspected normotensive hydrocephalus. In all cases, EI and Rout values were calculated (Fig. 1). Infusion tests performed on patients with secondary normal pressure hydrocephalus (NPH) (e.g., post-traumatic, posthemorrhagic,

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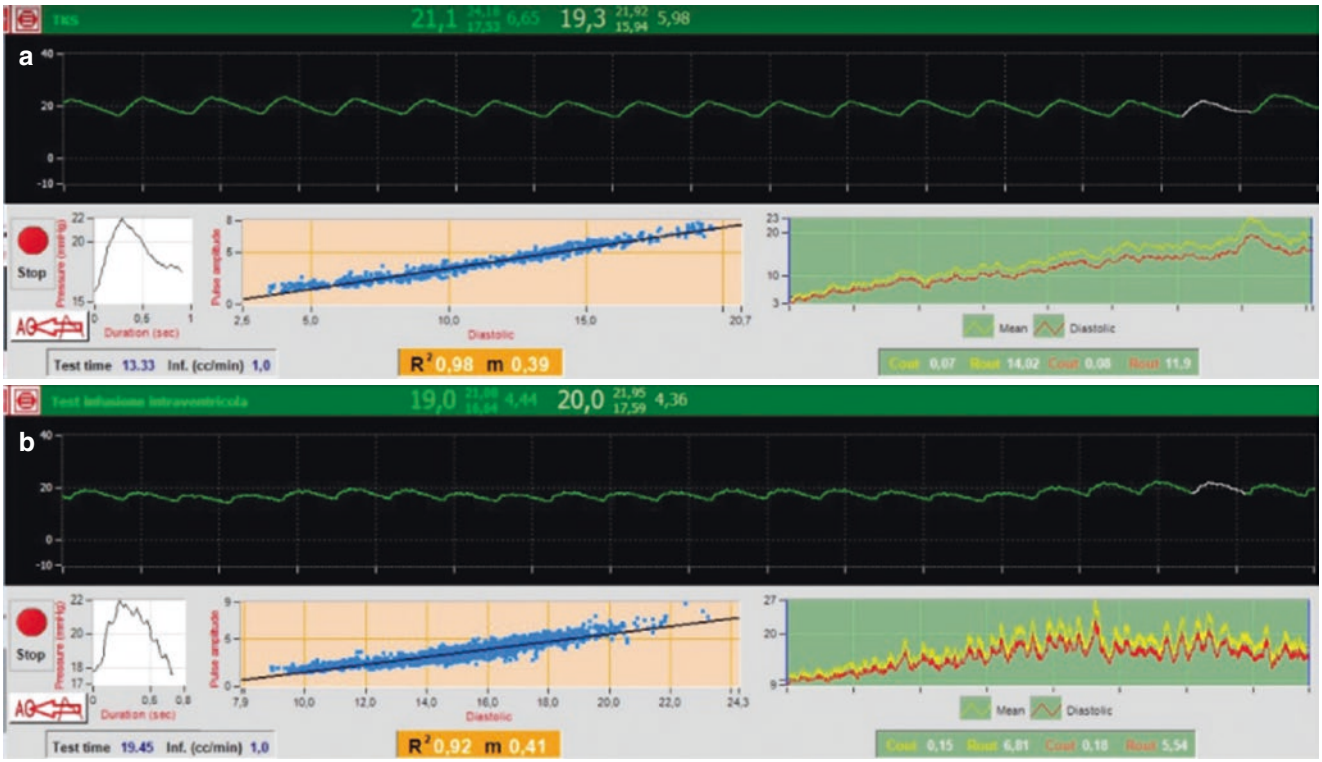


**Fig. 1** Examples of SKT (**a**) and IVKT (**b**) performed at our institution

or postinfective) or who showed evidence of long-standing overt ventriculomegaly (LOVA) were excluded.

The method used for the infusion test has been previously described [10]. All patients gave written informed consent for the analysis of clinical data. All iNPH patients were selected for the infusion test according to the evidence from partial or complete clinical trials and the radiological evidence of ventriculomegaly with increased Evan's ratios, disproportionally effaced superior frontal sulci, and reduced callosal angles at brain high-field MRI (≥ 1.5 tesla). All the patients also underwent preadmission neuropsychological testing conducted by dedicated neurologists. The decision to perform either a ventricular or a spinal infusion test was at the discretion of the neurosurgeon.

## 3 Data Collection

All the infusion tests were reviewed, and the following parameters were collected—opening pressure, closing pressure, IEI, Rout, and ICP wave morphology before infusion and at the end of infusion—according to the four classes. Classification was based on changes in the relations between the three ICP peaks (percussion, tidal, and dicrotic peaks) previously reported by our group [12].

## 4 Results

We analyzed 106 cases selected for suspected normotensive hydrocephalus: 52 patients underwent SKT, and the remaining 54 underwent IVKT (Table 1). Of the 40 patients in the SKT group with pathological elastance (71%), 17 also had a Rout >12 mmHg and 23 a Rout <12 mmHg. Of the 50 patients in the IVKT group with pathological elastance (92%), 38 also had a Rout >12 mmHg and 12 a Rout <12 mmHg. We have found a statistically significant difference between the presence of elastance and pathological Rout values, on one hand, and the presence of pathological elastance and nonpathological We have found a statistically significant difference between the presence of both pathological elastance and Rout values, on one hand, and the presence of pathological elastance and nonpathological Rout. Of the 12 patients in the SKT group with normal elastance (29%), four had a Rout >12 mmHg and eight a Rout <12 mmHg. Of the four patients in the IVKT group with normal elastance (8%), one had a Rout >12 mmHg and three a Rout <12 mmHg. In this case, we did not find a statistically significant difference between the presence of nonpathological elastance and Rout and the presence of nonpathological elastance and pathological Rout between the SKT group and the IVKT group ($p = 0.755$ Fisher exact test).

**Table 1** Results of both tests in patients with pathological values of IEI

| | IEI > 0.3 | IEI > 0.3 Rout >12 | IEI > 0.3 Rout <12 | *P*-value |
|---|---|---|---|---|
| IVKT | 50 | 38 | 12 | 0.001 |
| SKT | 40 | 23 | 17 | |

## 5 Discussion

The role of CSF dynamics, characterized by resistance to CSF outflow (Rout) and other pressure–volume compensatory parameters, is still controversial in NPH, partially reflecting the insufficiently understood regulatory mechanism of CSF production [13], making the diagnosis and management of idiopathic NPH a complicated issue.

The diagnosis of iNPH is primarily clinical and radiological. However, because the literature reported a percentage of shunt nonresponders, ranging between 20% and 40% of patients [14], some ancillary, invasive tests have been developed to help clinicians to select patients who are more likely to improve after surgical treatment [8, 14, 15].

The ancillary tests can be divided into two categories: subtraction tests, namely the tap test or prolonged lumbar drainage, and infusion tests, either lumbar or ventricular. Several studies have previously addressed the predictive role of these invasive tests: When specificity and positive predictive values are elevated, low-sensitivity and negative predictive values are generally reported [5, 15–18].

Whether lumbar tests and intraventricular tests are equally reliable or supplementary in providing the baseline CSF dynamic data of interest in patients with suspected iNPH is debated. A previous study [19] demonstrated that a lumbar infusion test equals the intraventricular one in the selection of shunt-responsive patients.

In other studies, an intraventricular infusion test was deemed more reliable than a lumbar infusion test [5] and allowed for obtaining deeper insights into the pathophysiology of iNPH [1].

Among the parameters studied during Katzman's infusion test, the CSF outflow resistance (Rout) is generally regarded as the most significant one to predict improvement after shunt placement [2, 3, 9]; however a multicenter study concluded that Rout should not be used as a parameter to exclude patients from treatment [5].

In 2010, our group summarized 30 years of experience in the treatment of iNPH, showing that an intracranial elastance index (IEI) above 0.3 was a robust predictor of a positive response after shunting [10]. This index was automatically computed by a dedicated software program developed at our institution by measuring the slope of the linear regression between each diastolic intracranial pressure (ICP) value and the corresponding amplitude of each CSF pulse pressure wave during an intraventricular infusion test. The test was considered as reliable if the coefficient of determination ($R^2$) was >0.8. All the patients who were selected for shunting using a threshold of IEI ≥ 0.3 showed clinical improvements at 6- and 12-month follow-ups. On the other hand, patients with an IEI < 0.3 did not improve at the same follow-up time points. In the same series, Rout values did not correlate with clinical outcomes.

More recently, we retrospectively reviewed 64 patients undergoing ventriculoperitoneal shunting for iNPH on the basis of a positive ventricular infusion test (IEI ≥ 0.3), and we found that an IEI ≥ 0.3 predicts both short-term and long-term outcomes, where more than 50% of patients were able to look after themselves 6 years after treatment [11].

IVKT, although more invasive than the SKT, allows a more reliable analysis of the CSF dynamics [20]. Our study, based on an analysis of instrumental data, highlights that in cases of IVKT, pathological elastance values are significantly related to the pathological ones of Rout, unlike the cases of the SKT group. This matching, not found for non-pathological values of elastance and Rout, could be considered a more reliable index of the overall significance of the test rather than a separate analysis of the same, thus providing evidence of the superiority of the IVKT.

## 6 Limitations

Our study could be prone to the biases associated with a retrospective research method. The limited number of cases further limits the strengths of this study. Moreover, the present study deals only with technical aspects of infusion tests; we did not consider clinical aspects or the predictive values of the test in terms of the outcomes of shunt procedures, so our findings should be analyzed with caution.

## 7 Conclusions

IVKT and SKT to date represent two useful tools in the diagnosis of normal pressure hydrocephalus. Despite being more invasive, IVKT, including both IEI and Rout analysis, could be considered more reliable than SKT and therefore could be reserved for the most controversial cases.

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