




# Treatment of Idiopathic Normal Pressure Hydrocephalus with a Novel Programmable Valve: Prospective Evaluation of Costs, Efficacy, and Safety

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## Abstract

**Objective** Programmable valves provide an equal or superior neurological outcome when compared with fixed pressure ones, with fewer complications, in treating idiopathic normal pressure hydrocephalus (iNPH) patients. Long-term costs of these treatments have not been properly compared in literature. We sought to compare costs, efficacy, and safety of 1-year treatment of iNPH patients with programmable valve Sphera Pro and a fixed pressure valve.

**Materials and Methods** A prospective cohort of iNPH patients treated with programmable valve was compared with a historical cohort of iNPH patients treated with fixed pressure valve. Our primary outcome was mean direct cost of treating iNPH up to 1 year. Efficacy in treating iNPH and safety were assessed as secondary outcomes.

**Statistical Analysis** Proportions were compared using chi-square or Fisher's exact tests. Normally distributed variables were compared using the Student's *t*-test or the Mann-Whitney's *U* test. Differences in the evolution of the variables over time were assessed using generalized estimating equations. All tests were two-sided, with an  $\alpha$  of 0.05.

**Results** A total of 19 patients were analyzed in each group (mean age 75 years, the majority male). Comorbidities and clinical presentation were similar between groups. Both fixed pressure and programmable valve patients had neurological improvement over time ( $p < 0.001$ ), but no difference was seen between groups ( $p = 0.104$ ). The fixed pressure valve group had more complications than the programmable valve group (52.6% vs. 10.5%, respectively,  $p = 0.013$ ). Annual treatment cost per patient was US\$ 3,820  $\pm$  2,231 in the fixed pressure valve group and US\$ 3,108  $\pm$  553 in the programmable valve group. Mean difference was US\$712 (95% confidence interval, 393–1,805) in favor of the programmable valve group.

**Conclusion** The Sphera Pro valve with gravitational unit had 1 year treatment cost not higher than that of fixed pressure valve, and resulted in similar efficacy and fewer complications.

## Keywords

- ▶ cost analysis
- ▶ efficacy
- ▶ normal pressure hydrocephalus
- ▶ safety
- ▶ ventriculoperitoneal shunt

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## Introduction

Idiopathic normal pressure hydrocephalus (iNPH) is a chronic syndrome characterized by gait disturbance, cognitive impairment, and urinary incontinence, affecting mostly the elderly.<sup>1-3</sup> Cardinal imaging features include enlarged ventricles, in association with high-convexity/midline tightness and Sylvian fissure enlargement.<sup>4</sup> The cerebrospinal fluid (CSF) drainage test (tap test) is useful for diagnosing iNPH and predicting the therapeutic effect of a shunt intervention.<sup>4,5</sup>

Ventriculoperitoneal shunt (VPS) provides better neurological outcome than endoscopic third ventriculostomy, and it is the gold-standard treatment for iNPH.<sup>6</sup> Lumboperitoneal shunt (LPS) appears to be beneficial as well, but larger studies are needed.<sup>7</sup> Programmable valves provide equal or superior neurological outcome to fixed pressure ones, with fewer complications and reoperations (12 vs. 32%, respectively).<sup>8-11</sup> These advantages raise the question whether, despite its higher cost per unit, programmable valve long-term treatment could be cost-effective in treating NPH patients.

To our knowledge, there is only one retrospective study that has compared the costs of treatment of NPH with these two types of valves, but it considered costs to comprise as only the costs of the valve unit and surgery.<sup>12</sup>

Here, we aim to compare costs, efficacy, and safety of 1 year treatment of iNPH patients with two different types of valves: a novel programmable valve (Sphera Pro) with gravitational unit and a fixed pressure valve.

## Materials and Methods

### Study Design

This prospective cohort included patients diagnosed with probable iNPH submitted to VPS with a novel programmable valve (Sphera Pro) with gravitational unit. It was compared with a historical cohort, composed by probable iNPH patients treated with a fixed pressure valve (Sphera Duo). Both groups were followed for 1 year.

### Participants

The adopted diagnostic criteria for probable iNPH followed the guidelines of the Japanese Society of NPH.<sup>4</sup> All patients were consecutively considered for eligibility. Inclusion criteria were diagnosis of probable iNPH and age 60 years or more. Exclusion criteria included diagnosis of secondary NPH, other associated dementia syndromes, malignancy, uncontrolled clinical comorbidities, lost to follow-up, or refusal, on the part of a family member or by the patient, to participate in the study.

The patients were recruited from the cerebral hydrodynamics clinics, at the Institute of Psychiatry of the Hospital das Clínicas of the Medical School of São Paulo University (HC-FMUSP), a public tertiary hospital in Brazil. Patients submitted to programmable valve VPS were operated over the period from January 2018 until May 2020, after signing an informed consent form. Data from patients previously submitted to fixed pressure VPS from January 2016 through December 2017 were collected from clinical charts.

The study was approved by the local ethics committee (CAPESQ 2.778.905).

### Tap Test

The tap test was performed in the preoperative period by withdrawing 50 mL of CSF.<sup>4</sup> Clinical evaluation was performed by a multidisciplinary team consisting of a neurosurgeon, a neuropsychologist, and a physiotherapist. Two additional evaluations were performed at 3 and 72 hours after lumbar puncture. Each evaluation consisted of six clinical scales: NPH Japanese Scale (► **Table 1**), Mini-Mental Status Examination (MMSE), The Berg Balance Scale (BERG), Functional Independence Measure (FIM), Dynamic Gait Index (DGI), and Timed Up and Go (TUG).<sup>13-18</sup> The tap test was considered positive when the patient improved 10% in at least two scales. The best result of the two post-tap test assessments was considered for comparison.

### Surgery

VPS was performed with the same surgical technique and the same main surgeon, who has an extensive experience in cerebral hydrodynamics surgeries, in both groups. A ventricular catheter inserted by a right precoronal burr hole (Kocher point) was connected to a valve attached to a distal catheter, which was inserted into the peritoneal cavity through an incision 2 cm superior and lateral to the umbilical scar, traversing the rectus abdominis muscle. Positioning of the valve was retroauricular. Anesthesia was general. Two types of valves were used, as follows.

**Table 1** NPH Japanese Scale

Grade	Definition
Gait disturbance	
0	Normal
1	Unstable, but independent gait
2	Walking with one cane
3	Walking with two canes or a walker frame
4	Walking not possible
Dementia	
0	Within normal range
1	No apparent dementia but apathetic
2	Socially dependent, but independent at home
3	Partially dependent at home
4	Totally dependent
Urinary incontinence	
0	Absent
1	Absent but with pollakisuria or urinary urgency
2	Sometimes only at night
3	Sometimes even during the day
4	Frequent

### Programmable Pressure Valve

Prospective cohort patients were treated with a programmable pressure valve (Sphera Pro) with gravitational unit (Sphera Gav), which was donated by a Brazilian company, HpBio. Special care was taken to place the gravitational unit in a line along the body-axis to ensure proper functioning in the upright position.

The valve and reservoir are made of polysulfone with a silicone coating and titanium connectors, while the antigravity device is composed of tungsten and ruby spheres that confer maximum resistance when patient is in the orthostatic position (►Fig. 1). The valve has eight different pressure settings (ranging from 1 to 21 cm H<sub>2</sub>O), and its rotor has two mechanical safety locks that move in opposite directions, avoiding deprogramming of the valve with 3 Tesla magnetic resonance imaging (MRI).

Based on Boon et al, who showed better neurological outcome with low-pressure valves than with medium-pressure ones (74 and 53%, respectively), an initial pressure of 3 cm H<sub>2</sub>O was chosen for all patients.<sup>19</sup> This same study showed a higher incidence of subdural effusions with low pressure valve, though. To minimize this complication, an antigravitational unit (Sphera Gav) of 15 cm H<sub>2</sub>O was attached to the valve.

### Fixed Pressure Valve

Historical cohort patients were treated with a fixed pressure valve without a gravitational unit (Sphera Duo), which is the one available for patients in the Brazilian public health

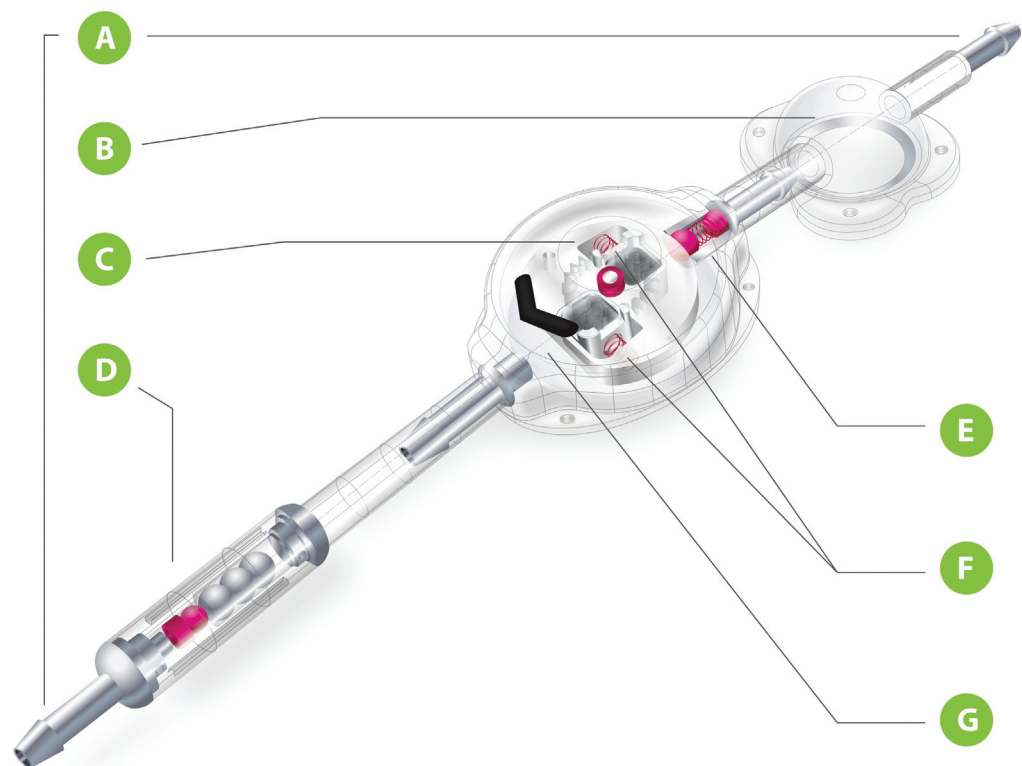
system. The chosen valve pressure was based on the final manometry value in the tap test, since it correlates to the neurological improvement seen after tap test. After the removal of 50 mL, a final pressure lower than 4 cm H<sub>2</sub>O resulted in the selection of a low-pressure valve; a final pressure between 4 and 10 cm H<sub>2</sub>O resulted in the selection of a medium-pressure valve; and a final pressure higher than 10 cm H<sub>2</sub>O resulted in the selection of a high-pressure valve.

### Follow-Up

Patients in both groups were followed for 12 months. Clinical (NPH Japanese Scale) and radiological (presence of subdural effusions) data were collected pre- and postoperatively (10 days, 3, 6, and 12 months). Imaging tests were evaluated by the same neuroradiologist in both groups. Length of hospital and intensive care unit (ICU) stays, as well as number of X-rays, computed tomographies (CTs), and MRIs were also recorded through 1 year. Complications such as CSF leak, infection, shunt malfunction, or overdrainage (subdural effusions) were strictly observed, treated, and recorded for later comparisons between groups.

### Costs

The costs were evaluated throughout 1 year of follow-up. Cost variables assessed through microcosting techniques (identification of actual individual resources used) were: number of surgeries, including reoperations; length of ICU and hospital stay, including readmissions; and number of imaging tests (X-rays, CTs, and MRIs) performed during



**Fig. 1** Programmable pressure valve (Sphera Pro) with gravitational unit (Sphera Gav). Constituents: (A) connectors, titanium; (B) reservoir for puncture with rigid base; (C) adjusting rotor with variable radius; (D) antigravity device with tungsten balls; (E) Sphera pressure control mechanism; (F) double locking system with neodymium magnets and springs; (G) silicone valve cover.

inpatient and outpatient care. The costs of imaging tests were: per X-ray, US\$ 27.40; per CT scan, US\$ 51.87; and per MRI exam, US\$ 102.83.

Macrocosting techniques were used to define daily ward (US\$ 237.35) and ICU (US\$ 667.81) charges and operating room costs per surgery (including medications, supplies, surgical, and anesthesiologist fees; excluding shunt systems)—US\$ 723.40. These values were originated from an average of all hospitalizations and surgeries performed in 2020 in our neurosurgical department, calculated by our financial department. Fixed pressure valve cost was US\$ 137.00. Programmable valves were donated for this study, but we assumed a cost of US\$ 1,346.15 per unit for the purposes of this study, since this is the sale price for private hospitals in Brazil.

Since we compared two groups in different periods of time, 2020 charges for laboratorial and imaging tests and hospital and medical fees were used. Costs were recorded in local currency (Brazilian reais) and converted to U.S. dollars, at the December 2020 exchange rate of US\$ 1 = R\$ 5.20.

### Outcomes

Our primary outcome was the mean direct cost of treating iNPH up to 1 year. Efficacy in treating iNPH, measured by mean NPH Japanese Scale, and safety, measured by complications rates, were assessed as secondary outcomes.

### Sample Size

A pilot study with 10 iNPH patients submitted to fixed pressure VPS was conducted in our institution in 2016. These patients were followed for 1 year. The 1-year average cost per patient was US\$ 3,240.65, with standard deviation (SD) US\$ 1,274.64.

Since the efficacy of a programmable valve is at least similar to that of fixed pressure valves, we assessed costs with a noninferiority study design.<sup>8–11</sup> Assuming a maximum difference of US\$ 1,038 per patient in favor of the programmable valve group (noninferiority margin), with

power 80% and  $\alpha$  0.05, 19 patients would be needed in each group. This US\$ 1,038 cost is an estimative of hospital costs for a complication with no need for reoperation, and includes the following charges: one inpatient day, one ICU day, two X-rays, and one head CT scan. We did not consider the reoperation cost because we wanted a more conservative noninferiority margin. To account for up to 10 to 20% losses, we planned to include 21 to 24 patients in each group.

This calculation was made with R software version 3.6.3 (package “SampleSize4ClinicalTrials” version 0.2.2).

### Statistical Analysis

Categorical variables were described as absolute and relative frequencies. Continuous variables were assessed for normality through kurtosis and skewness. If normally distributed, mean and SDs were used, and if not, median and quartiles were used. Proportions were compared using chi-square or Fisher's exact tests, as appropriate. Normally distributed variables were compared using the Student's *t*-test, and otherwise with the Mann–Whitney's *U* test.

Differences in the evolution of the NPH Japanese Scale score, Evans' index, and callosal angle over time were assessed using generalized estimating equations.

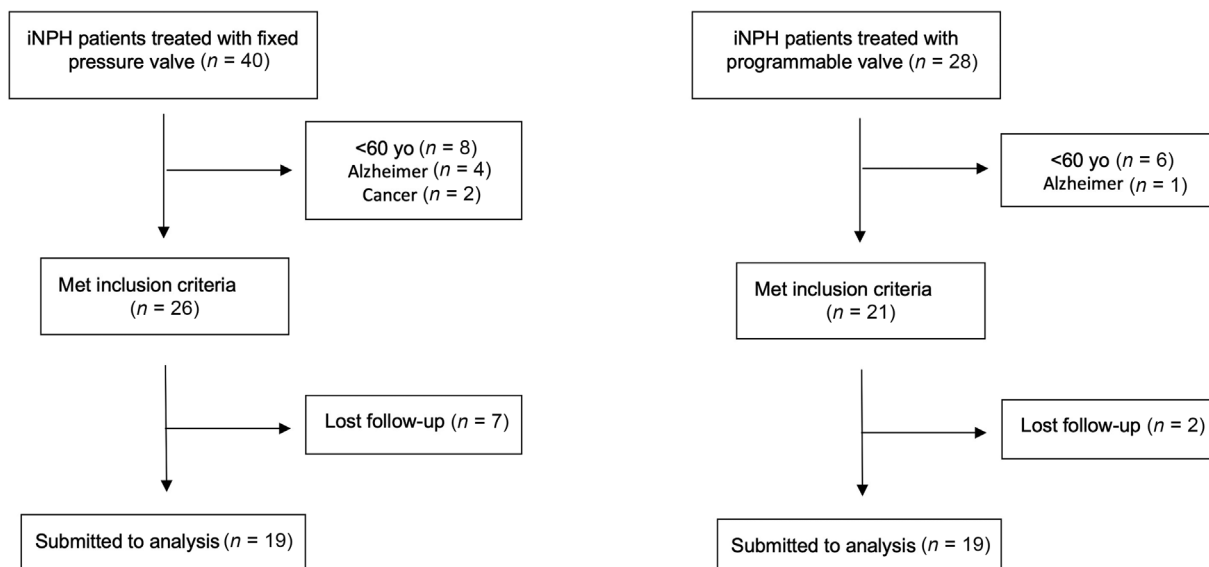
All tests were two-sided, with an  $\alpha$  of 0.05, and were performed with the Statistical Package for Social Sciences software (IBM SPSS Statistics for Windows 24.0, IBM Corp., Armonk, New York, United States).

## Results

### Participant Flow

As shown in ►Fig. 2, 40 patients with probable iNPH were submitted to a fixed pressure shunt in 2016 and 2017. Of these, 26 met the inclusion criteria, 7 patients were lost to follow-up and 19 patients were submitted to analysis.

Twenty-eight with probable iNPH were submitted to a programmable pressure shunt from January 2018 through



**Fig. 2** Enrollment of study subjects with fixed and programmable valves. iNPH, idiopathic normal pressure hydrocephalus; yo, years old.

**Table 2** Baseline characteristics, by valve type

Variable	Valve		p-Value
	Fixed pressure	Programmable	
Age	75.9 ± 7.6	75.7 ± 6.5	0.927
Male sex	14/19 (73.7)	10/19 (52.6)	0.179
Comorbidities	15/19 (78.9)	19/19 (100)	0.105
Clinical presentation			
Months from onset of symptoms	21.7 ± 19.0	31.3 ± 15.3	0.096
NPH Japanese Scale	6.6 ± 1.3	6.0 ± 2.0	0.302
Gait disturbance	19/19 (100.0)	19/19 (100.0)	–
Urinary incontinence	19/19 (100.0)	19/19 (100.0)	–
Cognitive impairment	17/19 (89.5)	16/19 (84.2)	> 0.999
Baseline imaging			
Evans' index	0.37 ± 0.04	0.34 ± 0.04	0.027
Callosal angle	78.7 ± 26.0	72.4 ± 15.3	0.364
Transependymal edema	7/19 (36.8)	5/19 (26.3)	0.485
Increased peak flow velocity through the aqueduct	4/12 (33.3)	3/15 (20.0)	0.662

Abbreviation: NPH, normal pressure hydrocephalus.

Note: Data presented as *n* (%) or mean ± standard deviation.

May 2020; 21 met the inclusion criteria, 2 patients were lost to follow-up and 19 patients were submitted to analysis.

### Baseline Data

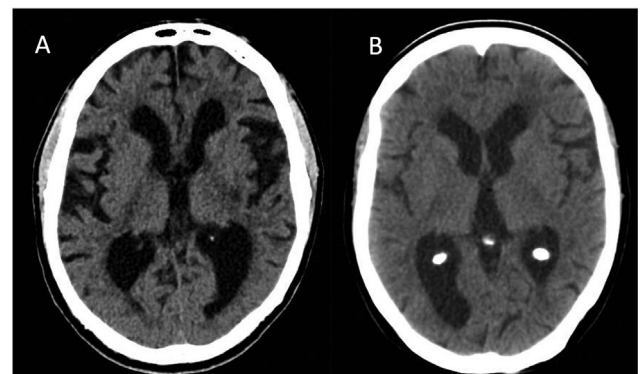
As shown in ► **Table 2**, the mean age was around 75 years and most patients were male in both groups. Comorbidities and clinical presentation were similar between groups. All patients had gait disturbance and urinary incontinence and most of them had cognitive impairment. Time from the onset of symptoms to the VPS tended to be longer for those submitted to the programmable shunt ( $31.3 \pm 15.3$  vs.  $21.7 \pm 19.0$ ,  $p = 0.096$ ).

For the fixed pressure valve patients, mean Evans' index was 0.37, and mean callosal angle was 78.6; transependymal edema was present in 36.9% of patients, while increased peak flow velocity through aqueduct was seen in 33.3% of patients. In the programmable pressure valve group, mean Evans' index was 0.34, and mean callosal angle was 72.4; transependymal edema was present in 26.3% of patients, while increased peak flow velocity through aqueduct was present in 20.0% of patients. The difference in Evans' index between groups was statistically significant ( $p = 0.027$ ). ► **Fig. 3** shows a CT scan of a typical subject of each group of treatment.

In the fixed pressure valve patients, 17 medium-pressure, 1 low-pressure, and 1 high-pressure valves were implanted.

### Efficacy

Preoperative mean NPH Japanese Scale was 6.6 ( $\pm 1.3$ ) among the fixed pressure valve group and 6.0 ( $\pm 2.0$ ) among the programmable pressure valve group ( $p = 0.30$ ). The NPH Japanese Scale assessment over time is presented in ► **Table 3**.



**Fig. 3** Skull computed tomography (CT) scan of a typical patient of the fixed pressure valve group (A) and of the programmable valve group (B). A large Evans' index and an enlargement of the cerebrospinal fluid spaces are seen in both patients.

NPH Japanese Scale score variation over time did not differ between groups ( $p = 0.104$ ). Patients in both groups had lower scores on NPH Japanese Scale over time ( $p < 0.001$ ). The NPH Scale score improved in 73.3% of the fixed pressure valve patients and in 88.2% of the programmable valve patients.

### Safety

Patients with the fixed pressure valve had more complications than patients with the programmable pressure valve: 52.6% versus 10.5%, respectively,  $p = 0.013$ .

In the fixed pressure valve group, 10 patients (52.6%) had surgical complications in 1-year follow-up. One (patient number 17 of the time series) had meningitis 2 months after VPS and was submitted to treatment with antibiotics and

**Table 3** NPH Japanese Scale assessment over time, by valve type

Scale/Index	Valve	Preop	10 d	3 mo	6 mo	12 mo	Interaction <i>p</i> -value
NPH Japanese Scale	Fixed pressure	6.6 ± 1.3	5.3 ± 1.8	5.1 ± 2.3	5.5 ± 2.3	5.3 ± 1.6 <sup>a</sup>	0.104
	Programmable	6.0 ± 2.0	4.5 ± 2.3	4.4 ± 2.6	4.0 ± 2.2	4.1 ± 2.2 <sup>a</sup>	

Abbreviations: NPH, normal pressure hydrocephalus; Preop, preoperative.

Note: Data presented as mean ± standard deviation. Generalized estimating equations model.

<sup>a</sup>The NPH Japanese Scale score variation over time for both groups was statistically significant ( $p < 0.001$ ).

shunt removal. Another patient (number 12 of the time series) was submitted to revision surgery due to misplacement of a distal catheter out of the peritoneal cavity. Eight patients (numbers 2, 5, 7, 9, 10, 13, 16, and 19 of the time series), all of them with medium-pressure valves, had over-drainage and were submitted to subdural hematoma drainage and replacement of the valve with a high-pressure one, 87.5% of them within 6 months of follow-up. Three of these patients had more than one reoperation: two were submitted to one more surgery latter on, one patient due to wound dehiscence and the other one for another replacement of valve; one patient had two more subdural hematoma drainage surgeries within 1 year.

One patient with a medium-pressure valve had recurrence of NPH symptoms after 11 months and was submitted to a valve replacement surgery for a low-pressure one. Of the programmable pressure valve patients, only two (10.5%) were submitted to reoperation, both for more than 1 cm symptomatic chronic subdural effusions diagnosed at 3 months of follow-up. They were patient number 16 and 18 of the time series. These valves were adjusted for a drainage pressure of 21 cm H<sub>2</sub>O. One patient had a nonsurgical subdural effusion diagnosed by CT scan within

3 months, and the valve adjusted for 6.5 cm H<sub>2</sub>O; the effusion was resolved 3 months later. Five patients had the valve's drainage pressure adjusted for 1 cm H<sub>2</sub>O due to lack of clinical improvement: three of these adjustments were made in 3 months, and two in 6 months.

There were no deaths in both groups.

### Costs

Annual cost of treatment in the fixed pressure valve group was US\$ 72,591, represented as follows: US\$ 28,042 (38.6%) for ward days, US\$ 6,010.26 (8.3%) for ICU days, US\$ 1,374.61 (1.9%) for X-rays, US\$ 6,467.92 (8.9%) for CT scans, US\$ 1,953.75 (2.7%) for MRIs, and US\$ 28,742.02 (39.6%) for surgeries. Annual cost of treatment in the programmable pressure valve group was US\$ 59,043, as follows: US\$ 12,070.07 (20.4%) for ward days, US\$ 0 for ICU days, US\$ 742.29 (1.3%) for X-rays, US\$ 3,440.91 (5.8%) for CT scans, US\$ 2,056.57 (3.5%) for MRIs, and US\$ 40,733.86 (69%) for surgeries.

► **Table 4** summarizes resource use in the two groups. Significant differences were reoperations ( $p = 0.002$ ), total ICU length of stay ( $p = 0.037$ ), and CT scans ( $p = 0.006$ ), which were fewer in the programmable valve group. Distribution of these variables is shown in ► **Fig. 4**.

**Table 4** Resource use, by valve type

Variable	Valve		<i>p</i> -Value
	Fixed pressure	Programmable	
Duration of surgery (min)	60 (50–75)	55 (50–60)	0.285
Reoperation			
Any, <i>n</i> (%)	11 (57.9)	2 (10.5)	0.002
Median, maximum	1, 3	0, 1	0.002
Ward length of stay (d)			
Total (including readmissions)	2 (2–12)	3 (2–3)	0.309
Min–max	1–22	1–5	–
ICU length of stay (d)			
Total (including readmissions)	0 (0–0)	0 (0–0)	0.037
Min–max	0–4	0–0	–
Imaging (count)			
X-ray	1 (0–3)	1 (1–1)	0.565
CT	5 (3–9)	3 (2–4)	0.006
MRI	1 (1–1)	1 (1–2)	0.808

Abbreviations: CT, computed tomography; ICU, intensive care unit; MRI, magnetic resonance imaging.

Note: Data presented as median (quartiles).

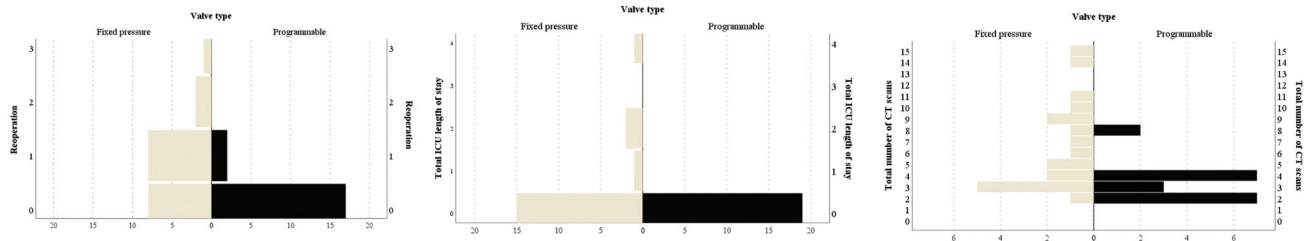


Fig. 4 Resource use, by valve type.

Annual treatment cost per patient was US\$ 3,820 ± 2,231 in the fixed pressure valve group, and US\$ 3,108 ± 553 in the programmable pressure valve group (► Fig. 5). Mean difference was US\$ 712 (95% confidence interval [CI], 393–1,805) in favor of the programmable valve group. There were two outliers in the programmable valve group and none in the fixed pressure valve group. After excluding these two values, annual treatment cost per patient was US\$ 2,935 ± 309 in the programmable pressure valve group, and the difference between groups was even higher: US\$ 885 (95% CI, 201 ± 1,957) in favor of the programmable valve group.

**Discussion**

Although LPS has also been described, VPS remains the most common surgical treatment for iNPH.<sup>20,21</sup> Here, we have described, for the first time, the efficacy, complications, and costs of iNPH treatment with the Sphera Pro valve with gravitational unit, and compared these results to a historical cohort of iNPH patients treated with a fixed pressure valve.

Regarding baselines characteristics, we adopt the view that the two groups were similar, and thus able to be validly compared. Although time from the onset of symptoms to the VPS tended to be longer for those submitted to the programmable shunt, this difference was not significant (*p* = 0.096). Evans’ index was different between groups, but it does not have a prognostic value in iNPH.<sup>22</sup>

Both groups had neurological improvement over time after VPS (*p* < 0.001), and the Japanese NPH scores did not differ between the groups (*p* = 0.104). These findings are in accordance with a recent meta-analysis, which showed similar efficacy (75%) of fixed pressure and programmable valves in treating iNPH.<sup>11</sup> The efficacy of the Sphera Pro valve with gravitational unit was similar (88.2%) in treating iNPH patients to that of other programmable valves: Oliveira et al showed efficacy of 83.33% with Strata, whereas Meier and Lemcke demonstrated an efficacy of 89% with Progav.<sup>10,23</sup>

We showed that the Sphera Pro valve with gravitational unit had fewer complications than fixed pressure valves: 10.5% versus 52.6%, respectively, *p* = 0.013. Complications

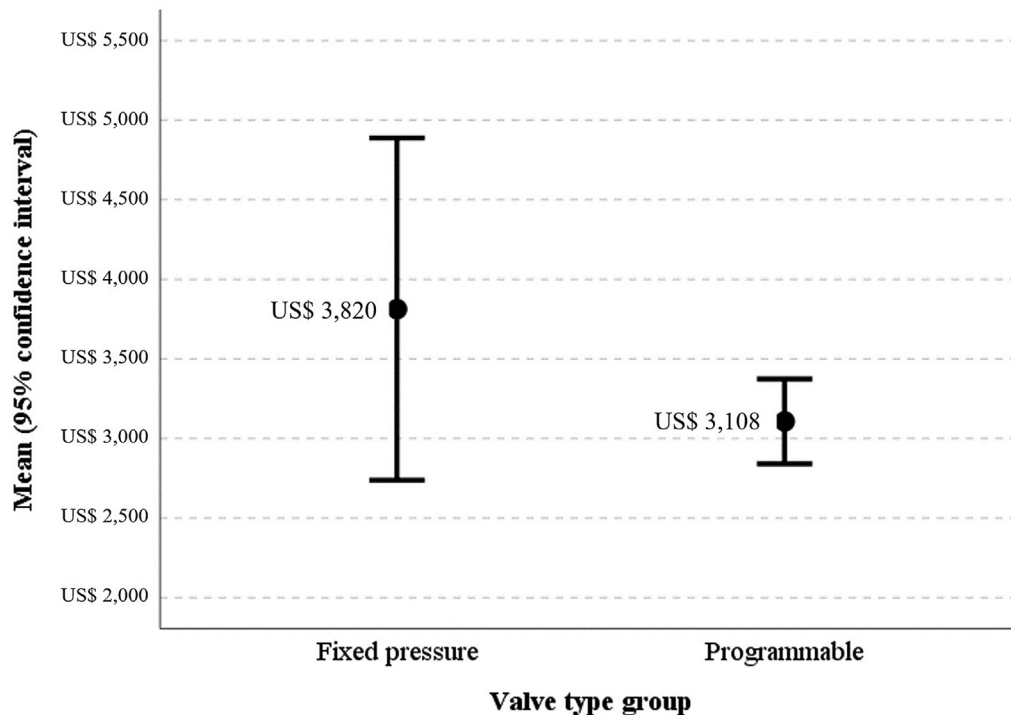


Fig. 5 Annual cost of treatment per patient, by valve type.

with fixed pressure valves in patients with NPH are indeed very common, with rates ranging from 13 to 40% in different studies.<sup>22</sup> Similarly, reoperation rates can reach 53% in 6 years of follow-up.<sup>22</sup> In the fixed pressure valve group of our study, two technical complications occurred in the second-half of the time series (patients number 12 and 17), while overdrainage complications occurred homogeneously during the time series (patients number 2, 5, 7, 9, 10, 13, 16, and 19), which indicates a lower risk of learning bias. Moreover, the overdrainage complications' rate in the fixed pressure valve group (42%) was very similar to that reported in literature: 71% among low-pressure valves and 34% in medium-pressure valves.<sup>19,24</sup>

Among programmable pressure valve patients, two (10.5%) were submitted to reoperation, both for chronic subdural effusions. This complication rate is similar to those described in NPH patients treated with other programmable valves.<sup>10,25</sup> Moreover, Giordan et al showed, in a recent meta-analysis, a 9% overdrainage rate with programmable valves.<sup>11</sup> Suchorska et al described, in a retrospective study, no surgical subdural effusion in 49 NPH patients treated with programmable valve and gravitational unit. This was probably due to an initial higher pressure (10 cm H<sub>2</sub>O) and higher gravitational unit (25 cm H<sub>2</sub>O) chosen by those surgeons.<sup>26</sup>

In our study, the programmable Sphera Pro valve with gravitational unit had similar efficacy and fewer complications than a fixed pressure valve in treating iNPH patients. These results are in agreement with previous studies with other types of programmable valves.<sup>10,11,23</sup> An important concern in relation to these valves, however, is their higher costs. Few studies have addressed this issue. Based on the results of SINPHONI and SINPHONI-2 trials, Kameda et al performed a cost-effectiveness analysis of treating patients with VPS and LPS with a programmable valve and found that the total cost for NPH patients will show a positive return on investment in periods as short as 18 months (VP), and 21 months (LP).<sup>7,27,28</sup>

Since the cost of a fixed pressure valve unit is lower than that of the programmable valve, some public health systems (such as the Brazilian system) provide only fixed pressure valve shunts without antigravitational unit for the treatment of NPH patients. Here, we have shown that the 1 year treatment cost with a programmable valve per patient (US\$ 3,108) was not higher than that with a fixed pressure valve (US\$ 3,820), the mean difference being US\$ 712 (95% CI, 393–1,805). Reoperation and ICU stay, which are important contributors for quality of life and health care, were also less frequent in the programmable valve group than the fixed pressure one, due to fewer complications. Agarwal et al showed a higher cost per patient when treating patients with different types of hydrocephalus with programmable pressure valves (US\$ 3,428 vs. US\$ 1,504).<sup>29</sup> This study had some important limitations, such as retrospective design, follow-up of 6 months, all types of hydrocephalus being included, and only valve unit costs being taken into consideration. A Turkish multicenter retrospective study showed a difference of US\$ 111 per patient when comparing NPH treatment with programmable and fixed pressure valves.<sup>12</sup> The authors considered only valve unit and surgical hour as costs, disregarding important factors such as number of ICU and ward days, and

imaging studies. Our study, therefore, provides the most complete comparison of cost, to date, between programmable and fixed pressure valves in the treatment of NPH patients. Moreover, since we showed that the costs of NPH using a programmable valve are not higher than those of treatment using a fixed pressure valve, our study may contribute to inclusion of programmable valves in NPH treatment protocols in public health systems worldwide.

Some limitations of our study should be addressed. In terms of diagnosis, we used the tap test due to its applicability and validity, as well as patient comfort, since it does not require hospitalization. Due to its limited sensitivity (26–61%), we may, though, have missed potential patients.<sup>30</sup> The cognitive assessment in tap test was performed with MMSE, which, although it has significant limitations, is a general tool used worldwide to assess dementia. Moreover, clinical improvement through time was assessed with NPH Japanese Scale in both groups. Although we used TUG, BERG, FIM, and DGI in tap test, we did not perform them during follow-up medical appointments, since their average length is 15 to 20 minutes in our hospital.

We compared a prospective cohort of patients submitted to VPS with programmable valves to a historical cohort of patients submitted to VPS with fixed pressure valves. Since it is well described in the literature that programmable valves have fewer complications than fixed pressure ones, it seemed to us antiethical to perform a prospective randomized study with both interventions.<sup>11</sup> We are aware of this design's limitations though: lack of control of exposure or outcome assessment, reliance on information from charts, which can lead to potential confounders, and that the retrospective aspect may introduce selection bias and misclassification or information bias.

According to Ijzerman and Creasey, we performed a full economic evaluation, since we compared two alternatives and considered both costs and consequences (efficacy, complications).<sup>31,32</sup> A cost-minimization analysis was then performed, since efficacy of both interventions was similar. Only direct costs were assessed, ignoring labor productivity and quality of life aspects. It is important to note that, since we compared costs of different periods of time, 2020 charges for laboratorial and imaging tests and hospital and medical fees were used, which may not reflect the present-day costs in both groups.

## Conclusion

The Sphera Pro valve with gravitational unit had 1 year treatment cost not higher than that of fixed pressure valve, and resulted in similar efficacy and fewer complications.

### Conflict of Interest

None declared.

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## References

- 1 Hakim S, Adams RD. The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. Observations on cerebrospinal fluid hydrodynamics. *J Neurol Sci* 1965;2(04):307–327
- 2 Factora R. When do common symptoms indicate normal pressure hydrocephalus? *Cleve Clin J Med* 2006;73(05):447–450, 452, 455–456 passim
- 3 McGirt MJ, Woodworth G, Coon AL, Thomas G, Williams MA, Rigamonti D. Diagnosis, treatment, and analysis of long-term outcomes in idiopathic normal-pressure hydrocephalus. *Neurosurgery* 2008;62(2, Suppl 2):670–677
- 4 Nakajima M, Yamada S, Miyajima M, et al. Guidelines for management of idiopathic normal pressure hydrocephalus (third edition): endorsed by the Japanese Society of normal pressure hydrocephalus. *Neurol Med Chir (Tokyo)* 2021;61:63–97
- 5 Mihalj M, Dolić K, Kolić K, Ledenko V. CSF tap test - obsolete or appropriate test for predicting shunt responsiveness? A systemic review. *J Neurol Sci* 2016;362:78–84
- 6 Pinto FCG, Saad F, Oliveira MF, et al. Role of endoscopic third ventriculostomy and ventriculoperitoneal shunt in idiopathic normal pressure hydrocephalus: preliminary results of a randomized clinical trial. *Neurosurgery* 2013;72(05):845–853, discussion 853–854
- 7 Kazui H, Miyajima M, Mori E, Ishikawa MSINPHONI-2 Investigators. Lumboperitoneal shunt surgery for idiopathic normal pressure hydrocephalus (SINPHONI-2): an open-label randomised trial. *Lancet Neurol* 2015;14(06):585–594
- 8 Zemack G, Romner B. Adjustable valves in normal-pressure hydrocephalus: a retrospective study of 218 patients. *Neurosurgery* 2002;51(06):1392–1400, discussion 1400–1402
- 9 Zemack G, Romner B. Seven years of clinical experience with the programmable Codman Hakim valve: a retrospective study of 583 patients. *J Neurosurg* 2000;92(06):941–948
- 10 Oliveira MF, Saad F, Reis RC, Rotta JM, Pinto FC. Programmable valve represents an efficient and safe tool in the treatment of idiopathic normal-pressure hydrocephalus patients. *Arq Neuropsiquiatr* 2013;71(04):229–236
- 11 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* 2018. Doi: 10.3171/2018.5.JNS1875
- 12 Serarslan Y, Yilmaz A, Çakır M, et al. Use of programmable versus nonprogrammable shunts in the management of normal pressure hydrocephalus: a multicenter retrospective study with cost-benefit analysis in Turkey. *Medicine (Baltimore)* 2017;96(39):e8185
- 13 Lopes MIR, Tornai JB, Jeng FLM, et al. Development of the Brazilian Portuguese version of the “Grading scale for idiopathic normal pressure hydrocephalus”: cross-cultural adaptation, reliability and validity. *Arq Neuropsiquiatr* 2018;76(10):692–696
- 14 Brucki SM, Nitrini R, Caramelli P, Bertolucci PH, Okamoto IH. Suggestions for utilization of the mini-mental state examination in Brazil. [in Portuguese]. *Arq Neuropsiquiatr* 2003;61(3B):777–781
- 15 Miyamoto ST, Lombardi Junior I, Berg KO, Ramos LR, Natour J. Brazilian version of The Berg Balance Scale. *Braz J Med Biol Res* 2004;37(09):1411–1421
- 16 Riberto M, Miyazaki MH, Jorge Filho D, Sakamoto H, Battistella LR. Reprodutibilidade da versão brasileira da medida de independência funcional. *Acta Fisiátrica* 2001;8:45–52
- 17 De Castro SM, Perracini MR, Ganança FF. Dynamic Gait Index–Brazilian version. *Rev Bras Otorrinolaringol (Engl Ed)* 2006;72(06):817–825
- 18 Mendes GAS, de Oliveira MF, Pinto FCG. The timed up and go test as a diagnostic criterion in normal pressure hydrocephalus. *World Neurosurg* 2017;105:456–461
- 19 Boon AJ, Tans JT, Delwel EJ, et al. Dutch Normal-Pressure Hydrocephalus Study: randomized comparison of low- and medium-pressure shunts. *J Neurosurg* 1998;88(03):490–495
- 20 Matsubara T, Ishikawa E, Hirata K, et al. A new mechanism of cerebrospinal fluid leakage after lumboperitoneal shunt: a theory of shunt side hole–case report. *Neurol Med Chir (Tokyo)* 2014;54(07):572–577
- 21 McGovern RA, Kelly KM, Chan AK, Morrissey NJ, McKhann GM II. Should ventriculoatrial shunting be the procedure of choice for normal-pressure hydrocephalus? *J Neurosurg* 2014;120(06):1458–1464
- 22 Pujari S, Kharkar S, Metellus P, Shuck J, Williams MA, Rigamonti D. Normal pressure hydrocephalus: long-term outcome after shunt surgery. *J Neurol Neurosurg Psychiatry* 2008;79(11):1282–1286
- 23 Meier U, Lemcke J. First clinical experiences in patients with idiopathic normal-pressure hydrocephalus with the adjustable gravity valve manufactured by Aesculap (proGAV(Aesculap)). *Acta Neurochir Suppl (Wien)* 2006;96:368–372
- 24 Pinto FCG, Pereira RM, Saad F, Teixeira MJ. Performance of fixed-pressure valve with antisiphon device SPHERA(®) in hydrocephalus treatment and overdrainage prevention. *Arq Neuropsiquiatr* 2012;70(09):704–709
- 25 Bozhkov Y, Roessler K, Hore N, Buchfelder M, Brandner S. Neurological outcome and frequency of overdrainage in normal pressure hydrocephalus directly correlates with implanted ventriculoperitoneal shunt valve type. *Neurol Res* 2017;39(07):601–605
- 26 Suchorska B, Kunz M, Schniepp R, et al. Optimized surgical treatment for normal pressure hydrocephalus: comparison between gravitational and differential pressure valves. *Acta Neurochir (Wien)* 2015;157(04):703–709
- 27 Kameda M, Yamada S, Atsuchi M, et al; SINPHONI and SINPHONI-2 Investigators. Cost-effectiveness analysis of shunt surgery for idiopathic normal pressure hydrocephalus based on the SINPHONI and SINPHONI-2 trials. *Acta Neurochir (Wien)* 2017;159(06):995–1003
- 28 Hashimoto M, Ishikawa M, Mori E, Kuwana N. Study of INPH on neurological improvement (SINPHONI) Diagnosis of idiopathic normal pressure hydrocephalus is supported by MRI-based scheme: a prospective cohort study. *Cerebrospinal Fluid Res* 2010;7:18
- 29 Agarwal N, Kashkoush A, McDowell MM, Lariviere WR, Ismail N, Friedlander RM. Comparative durability and cost analysis of ventricular shunts. *J Neurosurg* 2018. Doi: 10.3171/2017.11.JNS172212
- 30 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* 2005;57(03):S17–S28, discussion ii–v
- 31 Ijzerman MJ, Creasey GH. Economic evaluation of neuro-prostheses: a review of outcome assessment and valuation techniques. *Technol Disabil* 2004;16:33–40
- 32 Mogyrosy Z, Smith P. *The Main Methodological Issues in Costing Health Care Services: A Literature Review*. York: The University of York; 2005