ICP Monitoring and Phase-Contrast MRI to Investigate Intracranial Compliance

A. Lokossou, O. Balédent, S. Garnotel, G. Page, L. Balardy, Z. Czosnyka, P. Payoux, and E.A. Schmidt

Abstract *Objective*: The amplitude of intracranial pressure (ICP) can be measured by ICP monitoring. Phase-contrast magnetic resonance imaging (PCMRI) can quantify blood and cerebrospinal fluid (CSF) flows. The aim of this work was to investigate intracranial compliance at rest by combining baseline ICP monitoring and PCMRI in hydrocephalus patients.

Materials and methods: ICP monitoring was performed before infusion testing to quantify ΔICP_rest at the basal condition in 33 suspected hydrocephalus patients (74 years). The day before, patients had had a PCMRI to assess total cerebral blood flow (tCBF), intracranial blood volume change (stroke volume SVblood), and cervical CSF volume change (the stroke volume CSV). Global (blood and CSF) intracranial volume change (ΔIVC) during each cardiac cycle (CC) was calculated. Finally, Compliance: C_rest = ΔIVC/ΔICP_rest was calculated. The data set was postprocessed by two operators according to blind analysis.

Results: Bland–Altman plots showed that measurements presented no significant difference between the two operators. ΔICP_rest = 2.41 ± 1.21 mmHg, tCBF = 469.89 ± 127.54 mL/min, SVblood = 0.82 ± 0.32 mL/cc, CSV = 0.50 ± 0.22 mL / cc, ΔIVC = 0.44 ± 0.22 mL, and C_rest = 0.23 ± 0.15 mL/mmHg. There are significant relations between SVblood and CSV and also SVblood and tCBF.

Conclusions: During "basal" condition, the compliance amplitude of the intracranial compartment is heterogeneous in suspected hydrocephalus patients, and its value is lower than expected! This new parameter could represent new information, complementary to conventional infusion tests. We hope that this information can be applied to improve the selection of patients for shunt surgery.

Keywords ICP monitoring · PCMRI · Physiological · Intracranial compliance · Rest · Hydrocephalus

Introduction

Hydrocephalus is associated with cerebrospinal fluid (CSF) dynamic disturbances [1, 2]. It is characterized by gait disturbance, urinary incontinence, cognitive impairment, and ventricle enlargement [3]. The guidelines for the management of patients with hydrocephalus recommend intracranial pressure (ICP) monitoring and infusion studies [4] and the placement of a shunt as the treatment of reference.

From ICP monitoring and infusion tests, many parameters, like resistance to CSF absorption (Ro), mean ICP wave amplitude (MWA), mean ICP, elastance coefficient or

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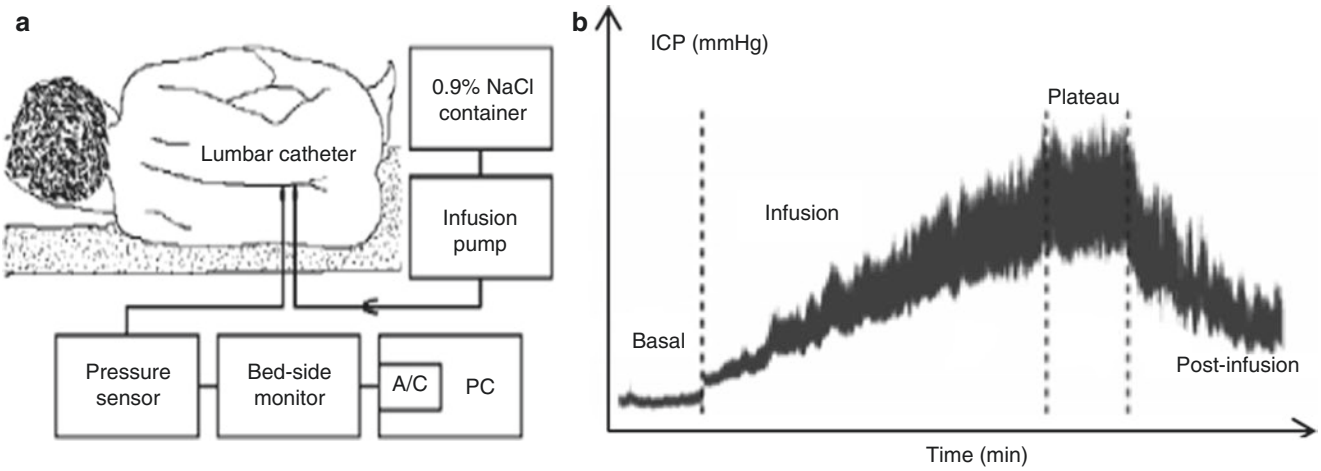

Fig. 1 (**a**) ICP monitoring system used during infusion test [15]. (**b**) Typical recording of mean ICP during constant-rate infusion test. Resting ICP was monitored at basal period. During infusion, ICP increases, reaches a plateau, and decreases after infusion

intracranial compliance, can be assessed. Some authors have suggested the usefulness of these parameters in identifying shunt responders [5], while others did not find this benefit [6]. Intracranial compliance determines the ability of the cranio-spinal system to accommodate an increase in volume without an increase in pressure [7, 8].

Intracranial compliance is obtained by dividing a known external volume infused in the subarachnoid spaces by the amplitude of ICP in response to this volume [9]. However, although this way of assessing intracranial compliance is recognized worldwide, it appears that infusion is a kind of disruption of intracranial volume [10] and does not reflect the physiological behavior of the intracranial compartment.

Phase-contrast magnetic resonance imaging (PCMRI) is the only imaging technique that is able to quantify the CSF and blood oscillations in physiological conditions during the cardiac cycle (CC) [11–13]. These volume changes are directly related to ICP oscillations during the CC [14].

We hypothesized that it was possible to calculate ICP changes during the CC before an infusion using ICP monitoring and to calculate intracranial volume change (blood and CSF) during the CC by PCMRI. The aim of this study was to quantify the intracranial compliance of hydrocephalus patients in physiological conditions without an infusion.

Materials and Methods

Study Population

Thirty-three patients suspected of probable hydrocephalus (15 women and 18 men) with a mean age of 74 ± 8 years (range 52–85) were prospectively included in the "Proliphyc" research program in Toulouse Hospital. They were included on the basis of chronic hydrocephalus symptoms: gait disturbance, cognitive impairment, urinary incontinence, and ventricular dilation. These patients underwent a lumbar constant-rate infusion test and PCMRI the day before.

ICP Study: Infusion Test Protocol

The lumbar constant-rate infusion test protocol described previously was used [15]. The test is performed with a constant-rate infusion (1.5 mL min^{-1}) using a lumbar catheter. The measuring system is presented in Fig. 1a. The lumbar catheter is connected to two needles: a pressure sensor and an infusion pump. A syringe infusion pump is connected to the second needle to infuse normal saline. After about 10 min of the basal pressure measurement, the infusion is started. The constant-rate infusion is continued until ICP reaches the plateau, and then the infusion is stopped. After infusion, the descending ICP is recorded for about 10 min (Fig. 1b). The signal is sampled, stored, analyzed, and displayed during the infusion test by using purpose-designed software ICM+ [16].

ICP Study: Postprocessing

We used homemade software to assess the resting ICP amplitude (ΔICP_rest) during the CC before the injection in the basal period (Fig. 1b). The software overcomes a patient's respiratory modulations and calculates the curve of evolution of ICP during the CC at rest. Then, ΔICP_rest was calculated during the rest period: $\Delta ICP\_rest = ICP_{max}\text{-}ICP_{min}$ (Fig. 2).

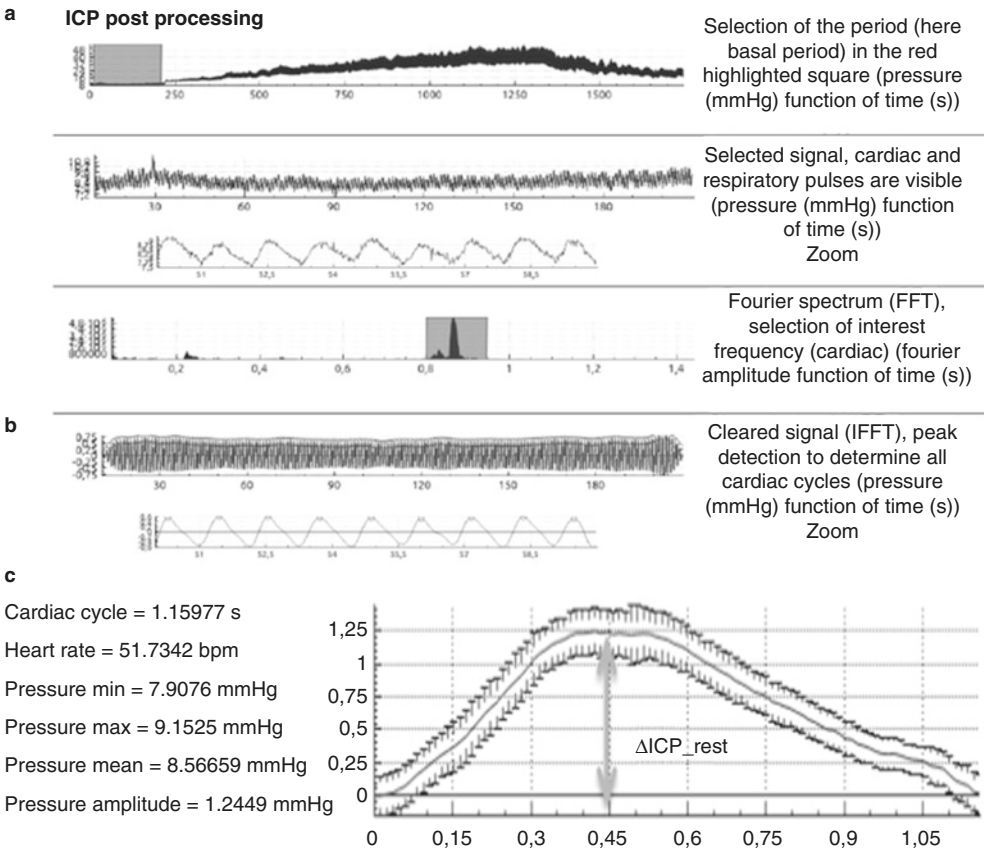

Fig. 2 Determination of resting ICP amplitude during CC. Using MRiCP software, we focus on basal ICP measurement (**a**); the software overcomes the respiratory modulations and focuses on patient cardiac frequency (**b**). Then, mean ICP with standard deviation was calculated over the entire CC, and the ICP amplitude at rest during the CC (ΔICP_rest) was also determined (**c**)

PCMRI Study: Flow Acquisitions

The same patients had PCMRI the day before the infusion test. It was performed on a 3T MRI machine. The PCMRI planes were perpendicular to the assumed direction of the CSF and blood flows to assess: (1) arterial blood flow in the internal carotid arteries (ICAs) and basilar artery (BA), and venous flow in the sinuses (sagittal and straight); (2) cervical CSF flow at the C2–C3 level. PCMRI parameters included a repetition time of 23 ms, echo time of 5 ms, a 150 × 150 mm field of view, a section thickness of 5 mm, and a flip angle of 15°. Velocity sensitization was set to 80 cm/s for the blood vessels and 5 cm/s for the CSF around the spine. Retrospective cardiac gating was used, and 32 images per CC were reconstructed. For each flow series, the acquisition time was approximatively 2 min, depending on the cardiac period (Fig. 3).

PCMRI Study: Flow Measurements

PCMRI acquisitions were postprocessed using flow analysis software [11]. This software automatically determines the flow curve over the CC for a given region of interest. The flow in the left and right internal carotid and basilar arteries were added in each individual to determine the total cerebral blood flow (tCBF). The flows in the sagittal and straight sinuses were summed to obtain the measured cerebral venous outflow. Given that the entire cerebral venous outflow must equal the tCBF, the measured venous flow was corrected taking account of tCBF. Arteriovenous flow was determined by subtracting the corrected venous flow from the tCBF. Cervical CSF flow during the CC was also determined. Cervical CSF stroke volume (CSV) and blood stroke volume (SVblood) were calculated by integrating respectively the cervical CSF flow and arteriovenous flow along the CC. These stroke volumes correspond to the volume of fluid moving inside and outside the cranium during the CC and represent the area under and over the curves of the cervical CSF and arteriovenous flows, respectively (Fig. 4a).

Arteriovenous flow and cervical CSF flow were summed, and the global intracranial flow change in the system during the CC was obtained. This global intracranial flow change was integrated along the CC, and the global (blood and CSF) intracranial volume change (ΔIVC) during the same CC was calculated (Fig. 4b).

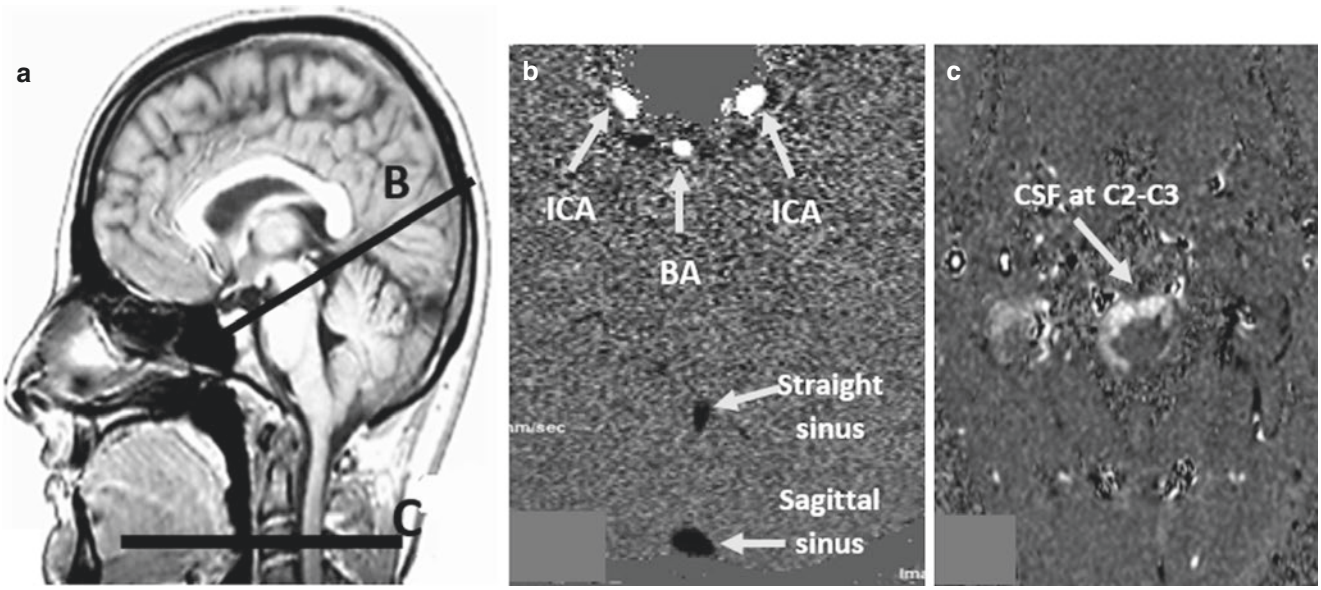

Fig. 3 (**a**) Data acquisition by PCMRI. The selected acquisition planes were perpendicular to the presumed flow direction. By convention, cranial–caudal flow was negative, whereas caudal–cranial flows were positive. Sections through the intracranial level (**b**) were used to quantify flows in right and left internal carotid arteries (ICAs), basilar artery (BA), and sinuses (sagittal and straight); a section through the cervical level (**c**) was used to quantify CSF at C2–C3 around the spine

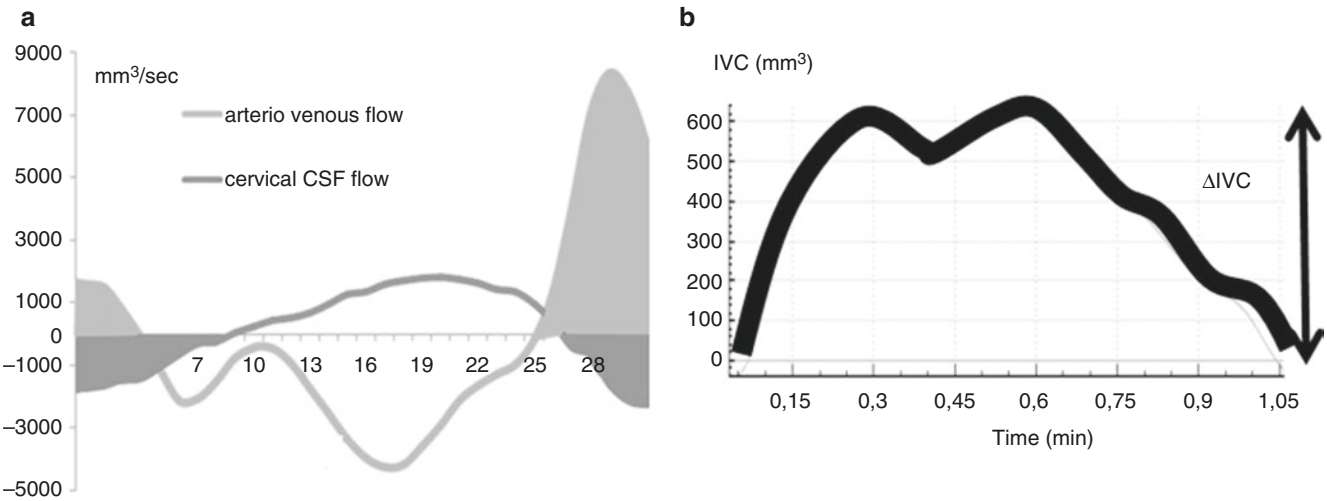

Fig. 4 (**a**) Arteriovenous and cervical CSF flow curves during CC. The areas under and over the curves represent the stroke volume. These two flows during the CC were summed and integrated, and global (blood + CSF) intracranial volume change (ΔIVC) was obtained (**b**)

Compliance of Intracranial Compartment

Finally, compliance at rest (C_rest) in mL/mmHg was calculated:

$$\mathrm{C\_rest} = \frac{\Delta \mathrm{IVC}}{\Delta \mathrm{ICP\_rest}}.$$

Statistical Analysis

Statistical analysis was performed using *R* statistical and *Excel* software. Two independent operators postprocessed these data by blinding analysis. To evaluate the agreement between the measurements (tCBF, ΔIVC, ΔICP_rest) performed by both of them, we used Bland–Altman plots and

Pearson correlation coefficients. After this step, we used the mean value of the measurements of both operators. We also determined the correlation between (1) tCBF and SVblood and (2) SVblood and CSV. Statistical significance was set at $p < 0.05$.

Results

The Bland–Altman plots showed that the measurements presented no significant difference between the two operators (Fig. 5). The Pearson correlation coefficient presented a good correlation between the measurements of the two operators: $r = 0.87$, $p < 0.001$; $r = 0.69$, $p < 0.001$; and $r = 0.96$, $p < 0.001$ for tCBF, ΔIVC, and ΔICP_rest, respectively. The mean value of two measurements were synthetized in Table 1. As shown in Fig. 6, there is a strong correlation between CSV and SVblood ($r = 0.76$, $p < 0.0001$) and between tCBF and SVblood ($r = 0.53$, $p < 0.001$). We found a heterogeneous value of compliance in our cohort: C_rest = 0.23 ± 0.15 mL/mmHg (range 0.04–0.63 mL/mmHg).

Table 1 Mean values and standard deviation of parameters calculated by two blind operators

Parameter	Mean value
tCBF (mL/min)	469.89 ± 127.54
CSV (mL/cc)	0.50 ± 0.22
SVblood (mL/cc)	0.82 ± 0.32
ΔIVC (mL)	0.44 ± 0.22
ΔICP_rest (mmHg)	2.41 ± 1.21

Discussion

This study proposes a new approach to assessing physiological intracranial compliance at rest in hydrocephalus patients.

First, our results showed that the quantification of intracranial volume change (ΔIVC) and resting intracranial amplitude (ΔICP_rest) could be acquired and calculated with good reproducibility even if the values are small. The obtained intracranial volume change during the CC is a small volume resulting from multiple measurements, which can generate additional errors. Nevertheless, the values obtained

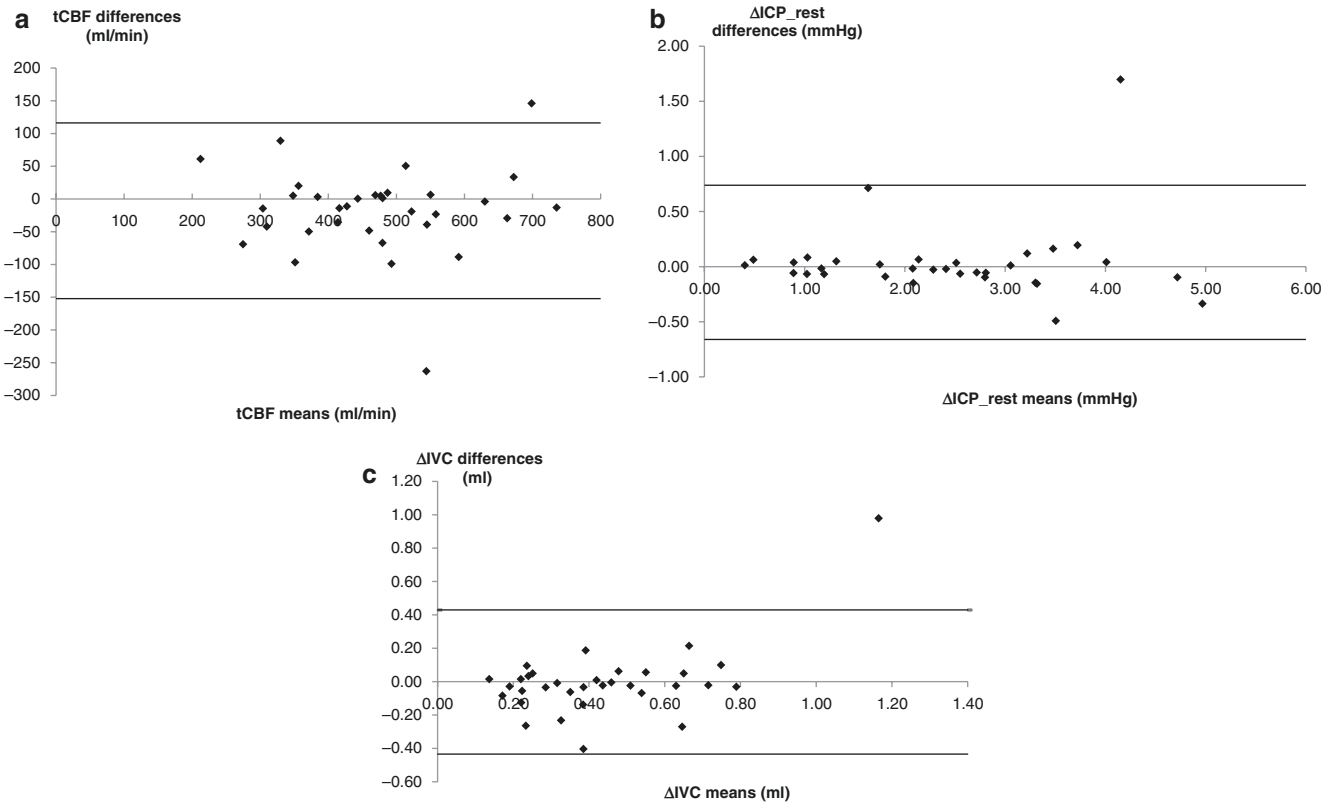

Fig. 5 Bland–Altman analysis plots of measurements performed by two independent operators for total cerebral blood flow (**a**), intracranial pressure amplitude at rest (**b**), and intracranial volume change (**c**). The difference between the two measurements lay with the limits of agreement, and the bias was close to zero for all estimations

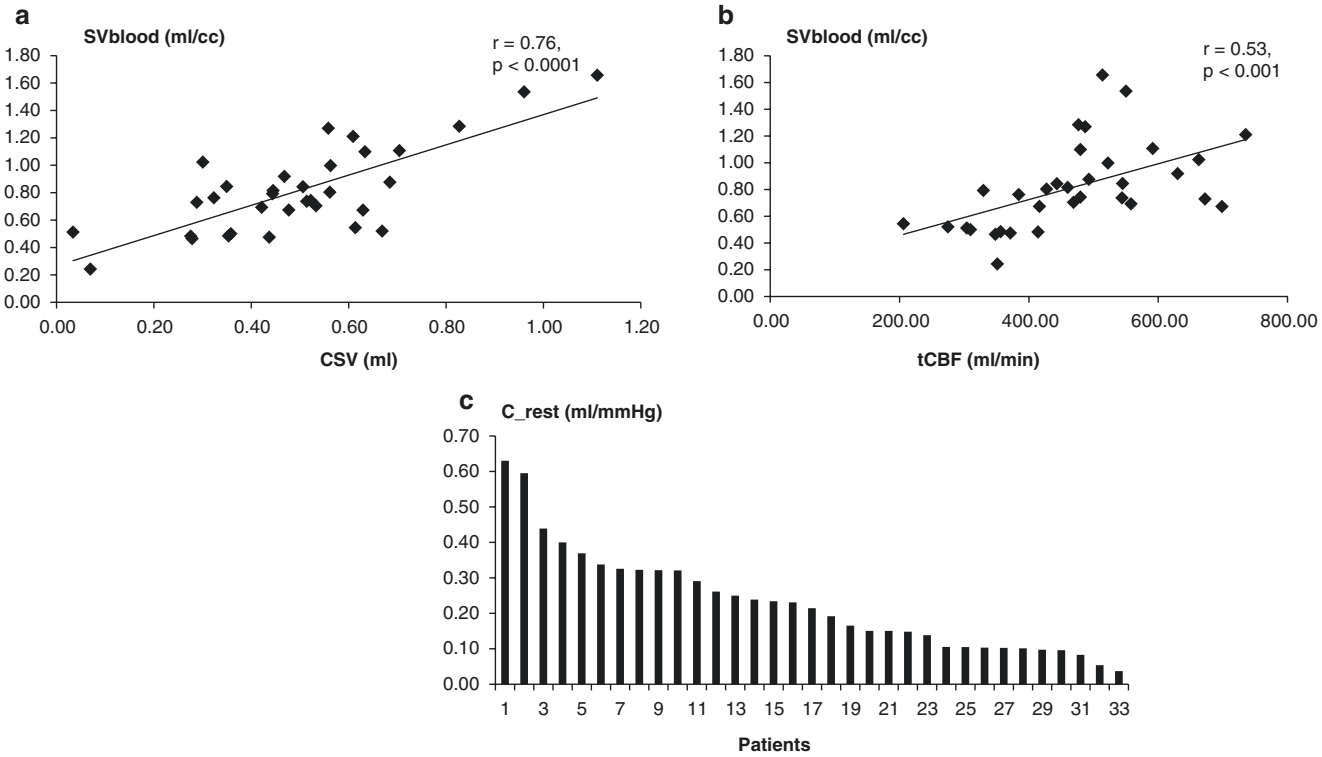

Fig. 6 (**a**) Correlation between arteriovenous stroke volume (SVblood) and cervical stroke volume (CSV) in patients. SVblood was positively correlated with CSV. (**b**) Correlation between SVblood and total cerebral blood flow (tCBF) in patients. SVblood was positively correlated with tCBF. (**c**) Compliance values at rest were heterogeneous in patients with suspected hydrocephalus

were in accordance with previous works [11, 17, 18]. Using a phantom, some authors have shown that PCMRI is an accurate technique for measuring small flow [18], while others have used this methodology to propose a noninvasive method to calculate ICP [17]. Another limit is that ICP monitoring and PCMRI were not performed at the same moment because ICP monitoring remains unavailable under MRI.

The mean value of compliance calculated at rest (C_rest = 0.23 ± 0.15 mL/mmHg) in our hydrocephalus patients was smaller than 0.5 mL/mmHg, a value that corresponds to altered intracranial compliance [19, 20]. C_rest was for the most part smaller than the values of intracranial compliance calculated using the infusion procedure in hydrocephalus patients (0.809 ± 0.085 mL/mmHg) [20] or in patients with severe head injury (0.68 ± 0.3 mL/mmHg) [8].

The differences in intracranial compliances observed may be related to the method used to measure intracranial compliance at rest. To measure C_rest, we used the intrinsic physiological intracranial volume change during the CC. Thus, this is a quick (1 s) and small volume change (less than 1 mL) in comparison with the infusion procedure. These results highlight the fact that intracranial compliance is a complex concept, and we hypothesize that intracranial compliance is time and volume dependent and use different mechanisms to maintain ICP mean value and amplitude.

The compliances calculated reflect the brain behavior at rest during one CC. In our population, we found heterogeneous values of C_rest. This indicates that the physiological intracranial compliance calculated could be a new biomarker to differentiate patients with hydrocephalus.

Taking into account that the patients included in this study underwent an infusion test, our future research will compare intracranial compliance at rest with other parameters like resistance to CSF absorption (Ro) and the following of patients. Future studies will seek for if physiological intracranial compliance may be helpful for selecting shunting patients.

Conclusion

This study shows that by combining the record of ICP monitoring at the basal period before injection and PCMRI, we are able to measure physiological intracranial compliance at rest. In hydrocephalus patients, this compliance is heterogeneous and lower than the impairment limit of compliance measured after infusion. This result indicates that the mechanism involved during a CC to respond to an increase in intracranial volume differs from that implicated during an infusion test.

Conflicts of interest statement We declare that we have no conflict of interest.

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