Neuromonitoring Using Neurosonography and Pupillometry in A Weaning and Early Neurorehabilitation Unit

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ABSTRACT

BACKGROUND AND PURPOSE: **Long-term surveillance of intracranial pressure (ICP) in neurological/neurosurgical patients during ventilator weaning and early neurorehabilitation currently relies on clinical observation because neuroimaging is rarely readily available. In this prospective study, multimodal neurosonography and pupillometry are evaluated for follow-up monitoring.**

METHODS: **Sonographic neuromonitoring was used to noninvasively examine patients' ICP during weaning and early neurorehabilitation. It allowed assessments of third ventricle width, possible midline shift, middle cerebral artery flow velocities, and bilateral optic nerve sheath diameters. Quantitative pupillometry was used to determine pupil size and reactivity. Other neuroimaging findings, spinal tap ICP measurements, and clinical follow-up data served as controls.**

RESULTS: **Seventeen patients—11 suffering from intracranial hemorrhage, four from encephalopathies, and two from ischemic stroke—were examined for ICP changes by using neurosonography and pupillometry during a mean observation period of 21 days. In total, 354 of 980 analyses (36.1%) yielded pathological results. In 15 of 17 patients (88.2%), pathological values were found during follow-up without a clear clinical correlate. In two patients (11.8%), clinically relevant changes in ICP occurred and were identified using neurosonography. Abnormal pupillometry findings displayed a high predictive value for absent clinical improvement.**

CONCLUSION: **Multimodal neurosonography may be a noninvasive means for long-term ICP assessment, whereas pupillometry may only detect rapid ICP changes during acute neurointensive care. The study also illustrates common pitfalls in neuromonitoring in general, with large numbers of pathological albeit nonsignificant findings. Additional controlled studies should validate the influence of detected subtle changes in ICP on neurological outcome.**

Keywords: Intracranial pressure, optic nerve sheath diameter, pupillometry, neurorehabilitation, neuromonitoring.

Acceptance: Received March 2, 2020, and in revised form May 25, 2020. Accepted for publication May 26, 2020.

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Acknowledgments and Disclosure: This study has been approved by the local Ethics Committee at the University of Regensburg (16-320-101) and consent to participate in the study was given by all patients or their legal guardians, if appropriate.
Authors' contributions to the study and preparation of the paper are as follows: study design (FS, BS, and DB), data acquisition (BS, AD, CG, DB, and FS), data analysis (BS, AW, RL, FS, and DB), initial draft of the manuscript (BS, DB, and FS), and final revisions to the paper (all authors).
All authors consented to publication of this paper in the current form.
On request, all data and materials will be made available for members of the editorial board.
Jo Ann M. Eliason, M.A., E.L.S.(D), edited this paper for English grammar and language.
There is no competing interest for any of the authors of this paper.
The study and preparation of the paper received no funding.

J Neuroimaging 2020;30:631-639.
DOI: 10.1111/jon.12742

Introduction

Repetitive invasive measurements of intracranial pressure (ICP) (such as measurements of intraparenchymal or intraventricular pressure obtained using a probe or ventricle drainage, or lumbar puncture [LP]), and neuroimaging with magnetic resonance imaging (MRI) and computed tomography (CT) are not practicable in dedicated ventilator weaning and early neurorehabilitation units (WENRUs), known in Germany as "neurorehabilitation intensive care units." The average hospital stay in a WENRU is 44.6 days after initial acute treatment.[1] It remains unclear whether there is an evidence-based benefit of routine invasive ICP measurements, and long-term implantable monitoring devices have not yet progressed beyond the experimental stage.[2-5] Also, cerebral MRI or CT is not often readily available within the WENRU, which can lead to unnecessary and sometimes risky transport of patients, especially ventilated patients, who lack clinical evidence for ICP elevations.[6] Thus, ICP surveillance is a diagnostic challenge in the WENRU, especially in patients in whom pathological changes in ICP may be relevant or have to be considered due to a particular brain injury such as following ventriculoperitoneal shunt placement.

Noninvasive ICP assessment may be obtained at the patient's bedside using transcranial and orbital sonography and automated quantitative pupil measurement. Single sonographic parameters, such as determination of third ventricle width, midline shift (MLS), middle cerebral artery (MCA) flow velocities, or optic nerve sheath diameters (ONSD), and pupil size and reactivity, are established during the acute phase.[7-11] Yet, the combination of these different parameters may increase an examination's sensitivity and specificity for changes in ICP and thus lead to more efficient care for patients in the intensive care setting.

The aim of this study was to evaluate the use of multimodal neurosonography and pupillometry as a noninvasive real-time bedside method in the long-term treatment of patients in the WENRU. Any routine cerebral imaging or LP puncture with pressure measurement as well as clinical follow-up can be used for a reference study.

Methods

Participation Criteria and Data Collection

The present study was approved by the Ethics Committee at the University of Regensburg (16-320-101) and was conducted in accordance with the requirements of the Declaration of Helsinki of the World Medical Association. Inclusion criteria limited participants to adult neurorehabilitation patients; excluded were patients without a sufficient temporal bone window and those with diseases confined exclusively to the peripheral nervous system. In addition, patients (or their legal guardians, if appropriate) had to provide written consent before participation in the study. Recruitment of patients usually took place 1 or 2 days after admission to the WENRU of the Department of Neurology at Regensburg District Hospital.

The planned investigation period per patient lasted 4 weeks, during which eight examinations of each patient were pursued. Clinically relevant data, such as the patient's sex, age, underlying disease, and clinical follow-up, were recorded on a data collection form. At each examination, transcranial B-mode sonography (TCS), transcranial color-coded sonography (TCCS), transorbital sonography (TOS), and pupillometry were performed. If control reference examinations, such as CT or invasive measurement of ICP (eg, LP), were performed in advance or as part of the regular treatment algorithm, the data obtained were compared with the results of the neurosonography and pupillometry studies. No additional CT or LP examinations were performed solely for the study; such examinations were added only if indicated by clinical criteria.

Technical Data of the Examination

TCS, TCCS, and TOS were performed using two color duplex machines, each equipped with a sector and a high-frequency linear array transducer (Philips CX50 with S5-1 and L12-3 transducer, and GE Logiq 7 with S3 and L11 transducer). TCCS and TCS were performed using a 1.5-3.5 MHz (GE Logiq 7 S3 transducer) and a 1-5 MHz sector (Philips S5-1 transducer) array transducer with the patient supine. The width of the third ventricle and any existing MLS were measured in the diencephalic plane at the level of the epiphysis, as previously described.[7,8] Pulsed-wave Doppler in TCCS was used to measure the flow velocities of the proximal MCA. Relevant settings, such as pulse repetition frequency, gain, and insonation angle, have already been described in detail.[10] Both systolic and end-diastolic maximum values were recorded to calculate the pulsatility index (PI) according to Gosling and King.[11] TOS was used to measure the ONSD using 3-11 MHz (GE Logiq L11 transducer) and 3-12 MHz (Philips L12-3 transducer) linear array transducers. The ultrasound transmit power was applied according to the ALARA ("as low as reasonably achievable") principle (ie, mechanical index <.23), as previously described.[12] For a reliable assessment of the ONSD, three measurements were made for each examination in order to calculate the mean value.

Pupillometry

Pupillometry was performed with the aid of the NeuroOptics® NPi™-200 pupillometer, a hand-held optical reader used to measure pupil size and reactivity, as previously described.[13] The device combines an infrared camera, a signal processor, and an LED light source. The automatically generated "Neurological Pupil index™" (NPi™) is based on an algorithm that compares the measured value with a basic model of pupil response to light and then grades the value on a scale from 0 to 5.

Control Examinations

Standard CT was performed using a Siemens Somatom Definition AS (Siemens Healthcare, Erlangen, Germany) CT and software with 4-mm slice thickness to evaluate the width of the third ventricle. The width was assessed on the axial image as the distance between the inner boundaries of both ventricle walls located in front of the pineal gland. The examination performed as described, and an opening pressure greater than 20 cm H_2O and below 6 cm H_2O was considered pathological.[14]

Statistical Analysis

The statistical evaluation included a descriptive analysis (including number [*n*], percentage, range, means, and standard deviation [SD]), median, quartiles (Q1 and Q3), interquartile range (IQR), and Pearson's correlation coefficient (*R*).

Results

Study Population and General Findings

During a median observation period of 21 days (Q1, 13 days; Q3, 25 days; range 7-118 days), we examined 17 patients: 11 suffering from intracranial hemorrhage, four from encephalopathies, and two from ischemic stroke. The median patient age was 62 years (Q1, 53 years; Q3, 72 years; range 32-80 years). Thirteen patients were males (76%). A median 8 examinations per patient (Q1, 6 examinations; Q3, 8 examinations; range 4-16 examinations) were performed, and 131 examinations in all were included in our analysis. On average, bedside examinations lasted 20-60 minutes depending on examination conditions, which included completing some examinations in patients with mechanical ventilation. The characteristics of patients are described in Table 1. An overview of the collected parameters is presented in Table 2.

In a single patient, changes in ICP over 16 days highly correlated with changes in third ventricle width and ONSD ($R = .93$) (Table 3, patient 14; Figs 1-3). Pupillometry did not provide sufficient evidence of pressure changes. In two of 17 patients (11.8%), we found clinically relevant changes in ICP

Table 1. Characteristics of Patients

Characteristic	*N* (%) or Median (IQR)	Minimum	Maximum	Range
Total number	17			
Age (years)	62 (53-72)	32	80	48
Sex–male	13 (76%)			
Diagnosis				
Intracranial hemorrhage	11 (65%)			
Encephalopathy	4 (23%)			
Ischemic stroke	2 (12%)			
Shunt	3 (18%)			
Number of measurements				
Total number	131			
Per patient	8 (6-8)	4	16	12
Follow up period per patient (days)	21 (13-25)	7	118	111

IQR, interquartile range; *N*, number.

Table 2. Median (IQR) Values, Minimums, Maximums, and Ranges of the Studied Parameters

Parameter	Median (IQR)	Minimum	Maximum	Range
Third ventricle (mm)	9.9 (8-12.2)	4.2	22.5	18.3
MLS (mm)	1.1 (.6-2.0)	.0	5.2	5.2
ONSD l (mm)	5.2 (4.8-5.7)	4.0	6.7	2.7
ONSD r (mm)	5.2 (4.8-5.7)	3.5	6.6	3.1
PI MCA l	1.11 (.95-1.31)	.64	2.16	1.52
PI MCA r	1.17 (.97-1.29)	.64	1.96	1.32
NPi^{TM} l	4.5 (4.1-4.7)	1.2	4.9	3.7
NPi^{TM} r	4.4 (3.8-4.7)	.7	4.9	4.2

IQR, interquartile range; l, left; MCA, middle cerebral artery; MLS, midline shift; NPi^{TM}, neurological pupil index; ONSD, optic nerve sheath diameter; PI, pulsatility index; r, right.

that could be detected by neurosonography and corresponding therapeutic treatments, such as LP, shunt adjustment, and shunt exchange (Table 3, patients 14 and 16). In 15 patients (88.2%), pathological values without clinical correlates were found during follow-up (Table 3). Of 980 values collected, 354 (36.1%) were pathological, as will be explained in more detail below. Clinical improvement or deterioration was extracted from the weekly multidisciplinary team protocol.

Third Ventricle Width and MLS

In all patients, the third ventricle could be well visualized from both sides. The median diameter of the third ventricle was 9.9 mm (Q1, 8 mm; Q3, 12.2 mm; range 4.2-22.5 mm; mean ± SD, 11.02 ± 4.33 mm). The average lateral difference was .64 ± .64 mm ($n = 262$). If CT took place within 7 days of the ultrasound examination and the patient did not display a clinical change, a good accordance between both methods could be shown (average difference: mean ± SD, .71 ± .45 mm; $n = 12$) (Fig 1). In 82.4% of patients (Table 3), a deviation from the age-dependent standard values of ventricle width (third ventricle >4.8 ± 1.9 mm [age 40 ± 13 years] and >7.6 ± 2.1 mm [age 68 ± 8 years]) was found in the follow-up of the study.[7] TCS revealed a relevant MLS (MLS >3.5 mm) in 17.7% of patients (Table 3), and this was monitored during follow-up (Table 3, patient 6; Figs 4 and 5).[20]

MCA Flow Velocities

In all patients, MCA flow velocities were measured and the PI was calculated. The median PI was 1.11 on the left side (Q1, .95; Q3, 1.31; range .64-2.16; mean ± SD, 1.23 ± .34) and 1.17 on the right side (Q1, .97; Q3, 1.29; range .64-1.96; mean ± SD, 1.24 ± .35 mm). In 88.2% of patients, the PI was pathologically increased (Table 3; PI ≥1.0).[16]

Optic Nerve Sheath Diameter

Intrarater reliability was high, as the three ONSD measurements per examination showed an average standard deviation of .19 mm ($n = 702$). The median ONSD was 5.2 mm on the left side (Q1, 4.8 mm; Q3, 5.7 mm; range 4.0-6.7 mm; mean ± SD, 5.24 ± .61 mm) and 5.2 mm on the right side (Q1, 4.8 mm; Q3, 5.7 mm; range 3.5-6.6 mm; mean ± SD, 5.19 ± .66 mm). The ONSD was pathologically increased unilaterally in 23.5% of patients and bilaterally in 35.3% of patients (ONSD >5.8 mm).[9,12,17]

Results of Pupillometry

Pupillometry could be performed properly in all but one patient who was restlessness. The median NPi^{TM} was 4.5 on the left side (Q1, 4.1; Q3, 4.7; range 1.2-4.9; mean ± SD, 4.2 ± .7) and 4.4 on the right side (Q1, 3.8; Q3, 4.7; range .7-4.9; mean ± SD, 3.9 ± 1.1). In 29.4% of patients, an abnormal pupil reaction was found (NPi^{TM} <3.0 and/or a lateral difference in NPi^{TM} ≥.7, Table 3).[13]

Discussion

In this study, we demonstrated the utility of multimodal neurosonography to characterize short- and long-term ICP changes during early neurorehabilitation, including in patients who were being weaned from mechanical ventilation. To the best of our knowledge, this is the first study performed to investigate the noninvasive long-term follow-up of ICP in a WENRU by using

Table 3. Characteristics and Main Findings

							CT findings[*1]	Ultrasound findings						Pupillometer findings		
Patient ID	Sex	Age	Diagnosis	Number of measure-ments	Follow up period (days)	Shunt	Third ventricle (mm)	Third ventricle[*2] (mm)	MLS[*3]	ONSD l[*2] (mm)	ONSD r[*2] (mm)	PI l[*2]	PI r[*2]	NPi^{TM} l[*2]	NPi^{TM} r[*2]	Clinical improvement[*4]
1	M	55	ICH	10	32		6.6 10.3	7.2-10.1		5.9-6.7	5.1-6.6	1.12 – 1.56	1.05 – 1.58	4.0-4.7	4.3-4.7	
2	M	62	IS	8	26		/	10.5-12.2		4.4-6.3	4.9-6.0	1.17-1.95	1.37-1.74	4.7-4.8	4.5-4.8	X
3	M	65	ICH	8	22	X	7.9	7.9-10.4		4.5-5.8	4.2-5.1	.91-1.28	.99-2.21	1.2-4.1	1.1-2.8	
4	F	70	SAH	8	23		10.7	8.8-10.8		4.4-5.1	4.0-5.1	1.05-1.67	.95-1.41	4.7-4.9	4.5-4.9	
5	M	41	SAH	7	18		/	9.1-10.0		4.2-4.7	3.8-5.1	.73-1.08	.74-1.08	4.6-4.9	4.5-4.9	X
6	F	32	IS	5	10		/	8.7-9.4	X	4.9-6.1	4.4-6.6	.52-.65	.47-.59	3.9-4.1	4.1-4.4	X
7	M	64	Encephalitis	8	23		6.6	6.7-9.3		5.3-6.4	5.0-5.9	1.09-1.84	1.12-1.28	4.4-4.8	4.3 –4.8	X
8	M	79	SDH	8	22		/	6.6-8.0	X	4.5-5.7	5.1-5.9	1.38-2.42	1.34-2.14	3.3-4.9	2.9-4.9	
9	M	78	SAE	4	7		/	8.9-10.5		5.2-5.9	5.6-5.7	.70-.93	.76-.98	/	/	X
10	M	73	ICH	8	21		10.7	10.4-12.0		4.6-5.2	4.2-5.5	1.32-2.02	1.26-1.99	4.4-4.9	2.4-4.3	
11	M	80	ICH	5	10		/	13.5-14.2		5.8-6.1	5.8-6.3	1.48-1.84	1.43-2.24	4.5-4.8	4.3-4.7	
12	F	59	SAH	9	28		/	5.5-7.6		4.9-6.0	5.1-6.0	1.00-1.41	1.00-1.38	4.0-4.7	.7-3.4	
13	M	35	Encephalitis	5	10		4.7	4.3-6.2		5.2-5.7	5.2-5.8	.97-1.26	.88-1.02	3.2-4.1	3.4-4.3	X
14	F	56	SAH	7	16	X	14.7	7.5-15.8		4.0-5.8	4.6-6.2	.63-1.07	.95-1.34	4.5-4.8	4.7-4.8	X
15	M	51	HIE	8	20		/	8.5-12.8		4.7-5.6	4.5-6.0	.82-1.19	.89-1.28	3.8-4.8	3.3-4.5	
16	M	68	SAH	16	118	X	20.5 21.9 20.3 18.9	19.0-22.5		4.2-5.5	3.5-5.8	.81-1.23	1.06-2.18	1.9-4.3	3.4-4.4	
17	M	62	SAH	7	21		/	11.1-13.1	X	5.0-5.5	4.4-5.2	.83-1.40	.78-1.28	4.3-4.7	4.6-4.8	X

F, female; HIE, hypoxic ischemic encephalopathy; ICH, intracerebral hemorrhage; ID, identification; IS, ischemic stroke; l, left; M, male: MLS, midline shift; NPi^{TM}, neurological pupil index; ONSD, optic nerve sheath diameter; PI, pulsatility index; r, right; SAE, sepsis-associated encephalopathy; SAH, subarachnoid hemorrhage; SDH, subdural hematoma.

[*1]Distance from sonography ≤7 days; [*2]Minimum – Maximum; [*3]MLS>3.5 mm; [*4]Medical and rehabilitative (physical therapy and occupational therapy) follow-up.

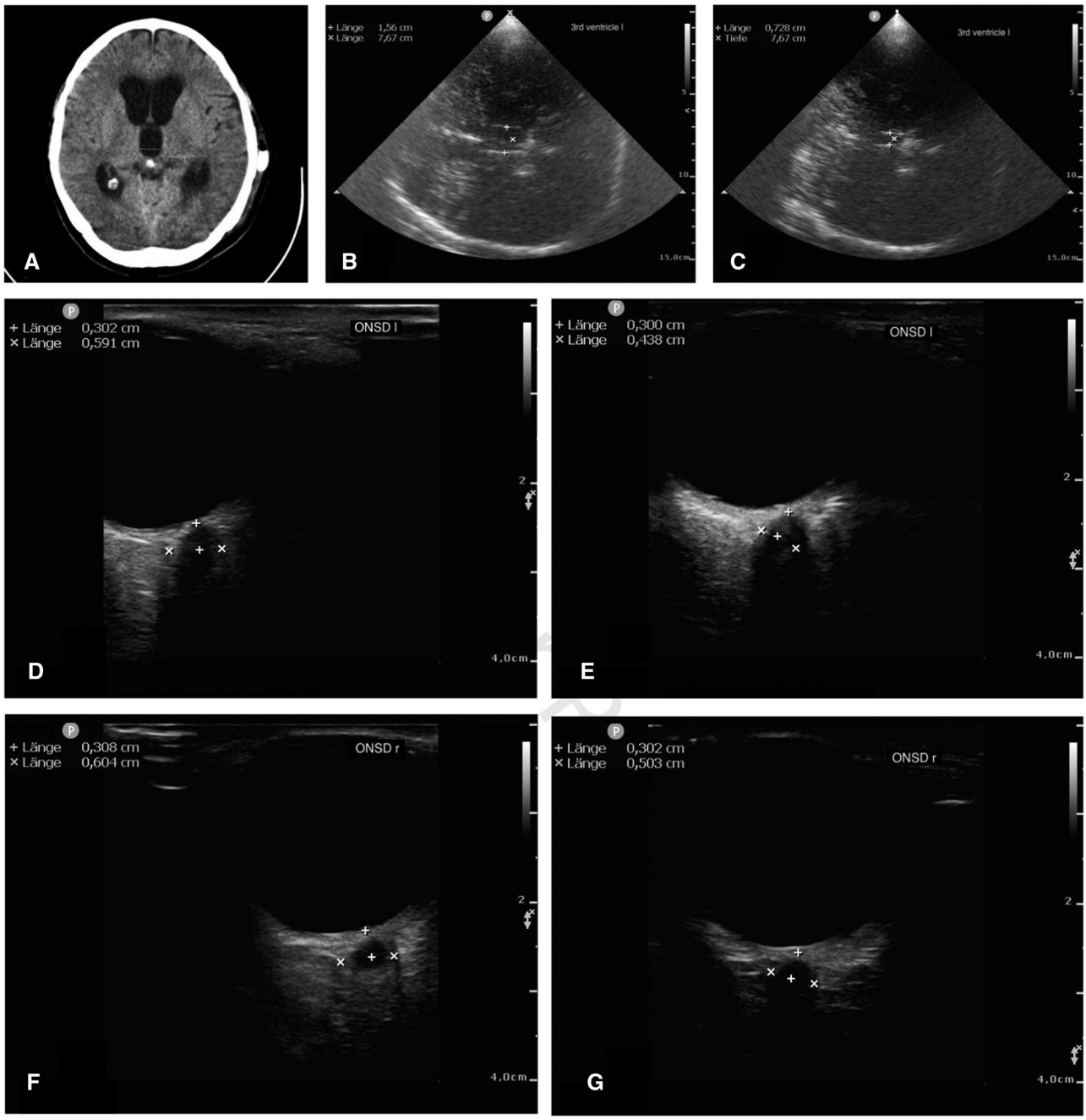
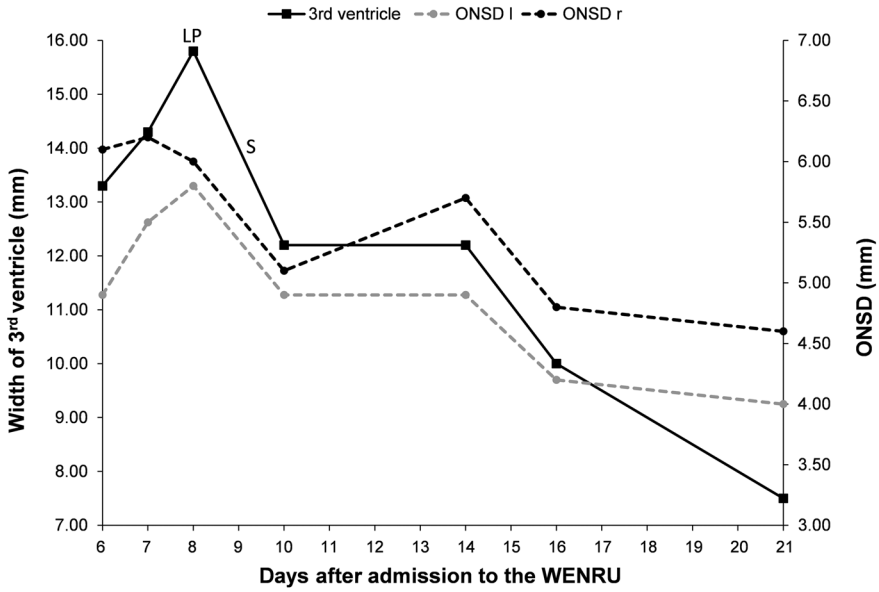


Fig 1. A 56-year-old female patient with a ventriculoperitoneal shunt following subarachnoid hemorrhage from a right posterior inferior cerebellar artery aneurysm and hydrocephalus occlusus, resulting in tetraparesis and severe neuropsychological defects. (A) CT at admission to the weaning and early neurorehabilitation unit showing a significantly dilated third ventricle (14.7 mm). (B) Transcranial B-mode sonography (TCS) on day 6 after admission: an increase in ventricle width to 15.6 mm. (C) TCS follow-up after 13 days of therapy (LP and shunting): width of third ventricle within normal parameters (7.3 mm). After therapy, the patient exhibited cognitive and motor improvements. Transorbital B-mode ultrasonography in the same patient: D (left) and F (right). Transorbital measurement of the ONSD day 6 after admission shows pathological values (5.9 mm, left eye; 6.0 mm, right eye). E (left) and G (right) Follow-up after 13 days of therapy (LP and shunting): width of the ONSD within normal parameters (4.4 mm, left eye; 5.0 mm right eye).

multimodal neurosonography and pupillometry. In a WENRU, as opposed to an acute neurology and neurosurgery intensive care unit, sudden and acute changes in ICP are rare events, invasive ICP measurements are absent, and cCT is frequently not readily available.

Sonographic measurement of the third ventricle is a well-established method.[7-9] In all 131 TCS examinations, we were able to identify and measure the third ventricle. In line with the clinical findings, elevations in ICP with concurrent changes in third ventricle width could be measured and, following a successful ICP-lowering therapy, decreases in ICP could be monitored–a finding in agreement with the report by Kiphuth et al.[18] Minimal deviations can be explained by (1) a time interval between the CT and TCS examinations and (2) the



Days	6	7	8	10	14	16	21
Width of 3rd ventricle (mm)	13.3	14.3	15.8	12.2	12.2	10	7.5
ONSD l (mm)	4.9	5.5	5.8	4.9	4.9	4.2	4
ONSD r (mm)	6.1	6.2	6	5.1	5.7	4.8	4.6

WENRU = weaning and early neurorehabilitation unit; ONSD = optic nerve sheath diameter; l = left; r = right; LP = lumbar puncture; S = shunting

Fig 2. Changes in the width of the third ventricle and the ONSD in the same patient over a period of 16 days.

higher resolution of TCS compared with CT. However, these differences were less than 1 mm and therefore not clinically significant.

Bedside TCS for an MLS is of high relevance especially in acute neurology, but also in the follow-up of patients with chronic intracranial pathologies; it displays high agreement with CT but can be repeated numerous times.[8,19-21] When an MLS was present, we were able to detect it and follow its course using TCCS in good accordance with findings on CT. Sonographic MLS evaluation is not only suitable for the acute stage of brain injury but also for long-term observation during the later course of the disease.

Blood flow analysis is an important adjunct for sonographic ICP measurements. Bellner et al were able to show a strong correlation between ICP measured with an intraventricular catheter and with the PI of the MCA.[22] Based on this assumption, we were also able to show a correlation between ICP and the PI of the MCA. Fortunately, none of the patients suffered from ICP elevation to the extent that cerebral blood flow was severely compromised, which is the normally strength of this technique. However, we also found no direct (time-related) correlation between the PI and the other measurements (third ventricle width, MLS, ONSD, or NPi^{TM}).

ONSD measurement is becoming increasingly popular as a noninvasive method of ICP evaluation in a variety of neurological diseases.[12,17,23-28] The reliability of sonographic ONSD measurements has been consistently rated according to published data in healthy individuals, and although there was no blinded review in our study, the supervising experienced neurologists (FS and DB) assured high quality.[29-31] An ONSD of >5.8 mm correlates well with an elevated ICP, and both increases and decreases in ICP are immediately measurable in the ONSD.[17,32] Using TOS, we detected pathological changes in the ONSD and measured increases or decreases in the diameter during follow-up. However, a formerly elevated ICP of >45 mmHg (ie, acute hydrocephalus from acute severe subarachnoid hemorrhage) can lead to structural changes within the ONSD and may lead to false-positive findings, stressing the importance for conducting a baseline TOS examination on patient admission.[33]

Another method of ICP diagnostic is pupillometry. Manual pupil measurements ("swinging flash light") show only a low interrater reliability, are important in acute neurology, and can be objectified with the aid of a pupillometer.[15,34] Using pupillometry, Chen et al were able to demonstrate a correlation between decreasing pupil response and increasing ICP, which proved to be a useful method for early assessment of patients with elevated ICP.[35] In patients during WENRU, we were able to detect changes in the ICP by using sonography and clinical findings, whereas no such correlation was apparent (or remained unnoticed) using pupillometry. This observation may be due to the small number of patients in our study, whose only moderately increased ICP occurred over a long period of time and had little influence on the sympathetic or parasympathetic nervous system, or to the use of cholinergic drugs, such as opiates or barbiturates. However, we did find a high correlation between an abnormal pupil response and the absence of clinical improvement: no clinical improvement (defined by medical and rehabilitative [physiotherapy and occupational therapy] follow-up) was found in any patients with a pathological NPi^{TM} ($n = 5$).

Clinical Relevance of Subclinical ICP Elevation

In our study, we detected subtle elevations in ICP without any apparent clinical deterioration. Current research on the

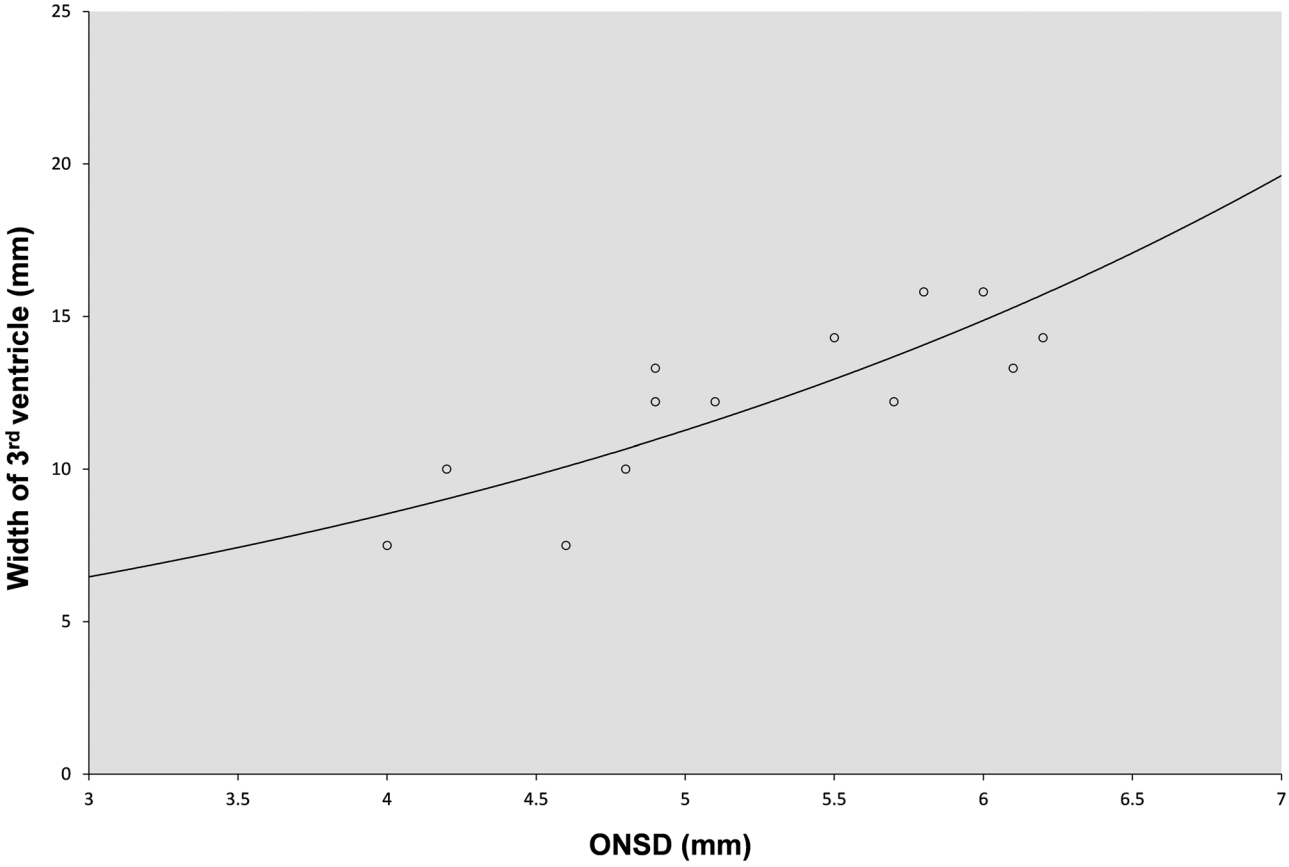


Fig 3. Correlation between the width of the third ventricle measured by transcranial sonography and the ONSD in the same patient.

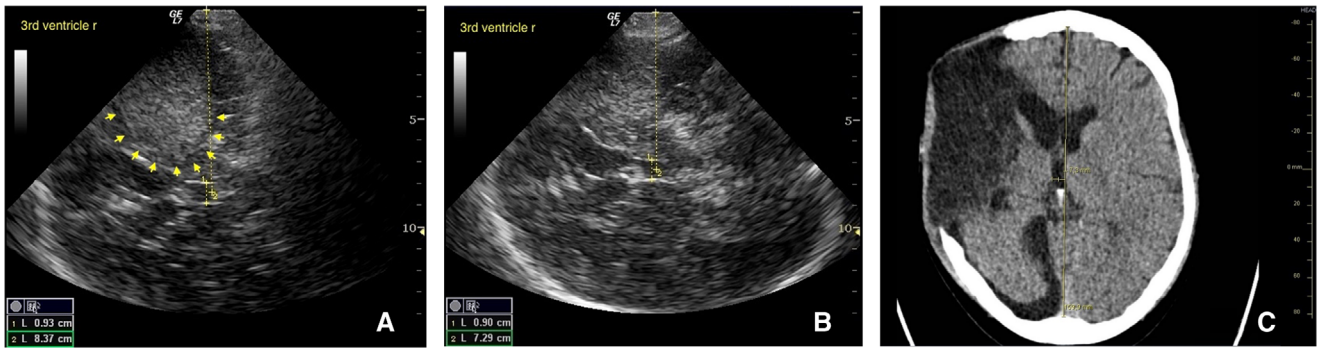


Fig 4. A 32-year-old female patient with craniectomy following space-occupying media infarction on the right side. (A-C) Course of midline shift (MLS) from the left to the right hemisphere. (A) Transcranial B-mode sonography (TCS) on day 4 after admission to the weaning and early neurorehabilitation unit: MLS of 1.6 mm to the left and marked right-sided hemorrhagic transformation. (B) TCS follow-up on day 14 after admission: decrease of the infarct with a mild nonsignificant MLS of 4.1 mm now to the right. (C) CT on day 25 after admission confirms a further decreasing MLS to the right.

perivascular spaces and brain interstitial fluid proposes a link between the microcirculation and brain detoxication.[36,37] Thus, any changes in ICP may influence long-term outcome in brain repair. Noninvasive ICP measurements have the potential to guide critically ill neurological patients through successful neurorehabilitation.

Strengths and Limitations of the Study

Sonography remains an examiner-dependent technique, and TCCS, not TCS, is dependent on the presence of a sufficient temporal bone window (especially in elderly women) and is thus subject to related inaccuracies. Nevertheless, bone defects due to trepanation allow for high-quality brain scans and should be exploited more frequently in early neurorehabilitation surveillance strategies. Standardized protocols, teaching efforts, and the use of an archive system for second opinions are possible solutions. Another limitation is the use of reference values in patients with severe brain injury and following prolonged acute intensive care medicine. These patients often show abnormal baseline values, and neurosonographic monitoring should be

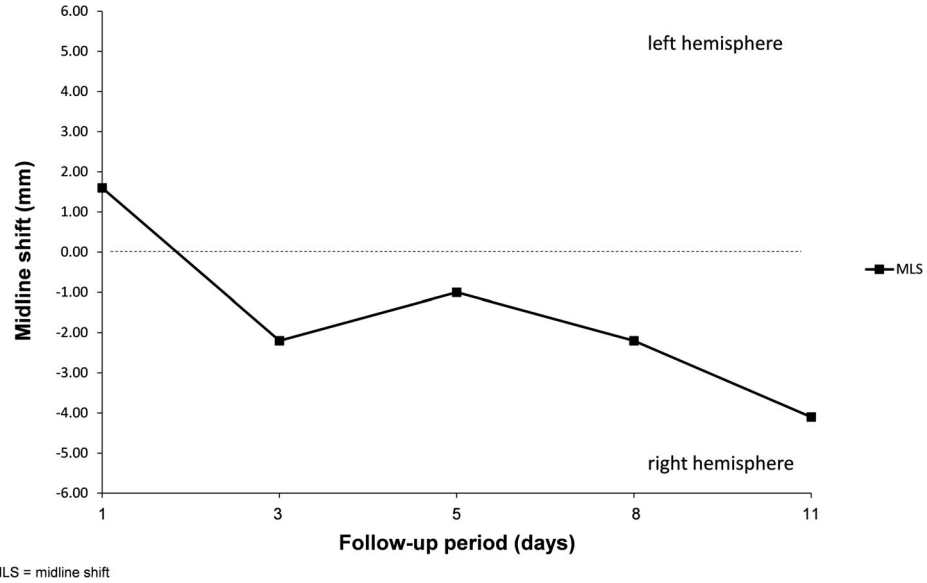


Fig 5. Course of midline shift from the left to the right hemisphere measured by transcranial sonography of the same patient.

normalized in timely association with the latest cCT and/or ICP measurements from the transferring acute clinic. Yet, clinical evaluation of patients with severe brain injury and prolonged coma also has limitations. Indices for a standardized assessment, such as the Barthel Index or the Extended Barthel Index, proved to be too imprecise to detect rapid ICP changes at an early stage and were therefore not used by us as an examination method. The strength of this study is the use of pure bedside and noninvasive diagnostics technique with no apparent side effects that are widely available in neurorehabilitation as opposed to cCT, MRI, or even direct ICP measurements. Patients with large bone defects are prime candidates for this kind of follow-up. A relevant limitation is our small and heterogeneous patient group and absent blinding; however, the investigator was not part of the treating team. Future large observational studies should be conducted to confirm our findings.

Conclusions

Our results show that multimodal neurosonography is suitable for noninvasive, repetitive assessment of ICP, especially in a WENRU, and can be a useful alternative to CT and LP in detecting complications from raised ICP. In addition, multimodal neurosonography may provide better insight into various aspects of the pathophysiology of neurological diseases. Pupillometry currently has greater significance when used to identify rapidly occurring ICP changes; in the future, it may serve as a predictive marker for the patient's clinical course. By combining different methods of measurement, changes in pressure could be detected more specifically, and the sensitivity of single measuring methods could be increased. Especially in cases of complex brain diseases, normal values should not be assessed as absolutes, but rather as comparative values within individuals during follow-up, so that complications can be detected earlier and therapy can be initiated. Therefore, we recommend that early validation of multimodal neurosonography using established imaging methods should be made upon WENRU admission to establish a baseline profile.

Outlook

Additional studies in larger numbers of patients in the WENRU are needed to determine whether multimodal sonography can serve as the doorkeeper for out-of-WENRU neuroimaging procedures and therapies. Further objectives should address moderate long- and short-term management of the ICP guided by sonographic neuromonitoring and their influence on long-term outcome in neurorehabilitation.

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