IRIS AperTO

UNIVERSITÀ DEGLI STUDI DI TORINO

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

Ultrasonography Monitoring of Optic Nerve Sheath Diameter and Retinal Vessels in Patients with Cerebral Hemorrhage

This is a pre print version of the following article:

Original Citation:

Availability:

This version is available http://hdl.handle.net/2318/1722565 since 2020-01-12T23:54:50Z

Published version:

DOI:10.1111/jon.12604

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

19 May 2024

Reliability of optic nerve sheath diameter and Doppler indices of retinal vessels in detecting and monitoring raised intracranial pressure of intracerebral haemorrhage

Andrea Naldi[a], Emanuele Pivetta[b], Lorenzo Coppo[c], Roberto Cantello[c], Cristoforo Comi[c], Alessandro Stecco[d], Paolo Cerrato[a], Martin Lesmeister[e], Piergiorgio Lochner[e]

Author affiliations:
[a] Stroke Unit, City of Health and Science University Hospital of Turin, Turin, Italy
[b] Cancer Epidemiology Unit and CRPT U, and Division of Emergency Medicine and High Dependency Unit, Department of Medical Sciences, University of Turin, Turin, Italy
[c] Neurology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[d] Radiology Unit, Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy
[e] Department of Neurology, Saarland University Medical Center, Homburg, Germany

Short title: Reliability of optic nerve sheath diameter and Doppler indices of retinal vessels in intracerebral haemorrhage

Title character count: 167
Number of references: 30; Tables: 3; **Figures:** 3
Word count abstract: 352; **Word count text:** 2600

Corresponding author:
Dr. Piergiorgio Lochner, Department of Neurology, Saarland University Medical Center, Kirrberger Str., 66421 Homburg, Germany
Phone +49 6841 16 14026, Fax +49 6841 16 24100 E-mail: piergiorgio.lochner@gmail.com

Abbreviations: intracerebral haemorrhage, ICH; intracranial pressure, ICP; optic nerve sheath diameter, ONSD; resistive index, RI; retinal venous pulsation, RVP

Key words (3-10):
Intracerebral haemorrhage; intracranial pressure; optic nerve sheath diameter; retinal vessels

Author disclosures:
Each author reports no conflicts to disclose.

ORCID

Abstract:

Background: Among the non-invasive methods for estimating increased intracranial pressure (ICP), the ultrasonography of optic nerve sheath diameter (ONSD) represents one of the most promising techniques; conversely, only few data are available about a possible diagnostic role of Doppler indices of retinal vessels.
Objective: Primary aim was to evaluate the diagnostic accuracy of optic nerve sheath diameter (ONSD) values compared with Doppler indices of central retinal artery and vein for the detection of elevated intracranial pressure (ICP) during the acute phase of intracerebral haemorrhage (ICH). The secondary aim was to establish the usefulness of a second assessment of the ONSD in the monitoring of ICH and to look for correlations between sonographic and radiological data.
Material and Methods: We consecutively enrolled 46 acute ICH patients with (group 1, n = 25) and without (group 2, n = 21) clinical and radiological CT signs of ICP and 40 healthy controls (control group). The median binocular ONSD and Doppler indices of retinal vessels including resistive index (RI) and retinal venous pulsation (RVP) were compared between the groups. Accuracy of the mentioned variables was estimated using cerebral CT scan results as reference, performed both at onset of ICH and over time depending on clinical conditions; correlations between sonographic parameters and haemorrhage volume and midline shift were assessed.
Results: Patients in group 1 had a significantly higher median binocular ONSD, RI and RVP values compared to other groups. Median binocular ONSD showed the higher accuracy for the detection of increased ICP (sensitivity, SE, and specificity, SPE, 100%; cut-off point ≥ 5.6 mm), while Doppler indices were less accurate (SE 48% and 80%, SPE 95% and 62% for RI and RVP respectively). In group 1, ONSD were significantly elevated both at onset of ICH than at control time (6.40 [0.60] and 6.00 [0.60] respectively). ONSD showed a good correlation with haemorrhage volume at onset of ICH (r=0.677, p=0.0002).
Conclusions: Median binocular ONSD evaluation showed a higher accuracy for the detection of elevated ICP compared with Doppler indices of retinal vessels. The ONSD enlargement observed in the early develop of ICH seemed to persist also over time.

Introduction

The mortality of patients with stroke due to intracerebral haemorrhage (ICH) is about 30-40% worldwide [1]. Baseline volume of ICH, intraventricular haemorrhage, haematoma expansion, and perihaematomal oedema are strongly predictive of worse prognosis and death, considering that increased intracranial pressure (ICP) leads to dislocation of midline structures and subsequently to axial brainstem herniation [2]. Therefore, the availability of both invasive and non-invasive tools for the estimation of ICP may improve the management of these vulnerable subjects. Compared with both the reference methods – intraventricular catheter and CT brain scan –, ultrasonography of the optic nerve sheath diameter (ONSD) is a simple, non-invasive, repeatable, and bedside technique for the detection of increased ICP [3,4] and thus particularly suitable in an intensive care or stroke-unit setting [5].

Recently two studies demonstrated the reliability of ultrasonography of ONSD to identify raised ICP in intracranial haemorrhage patients [6,7], but only one case series assessed the possible role of serial measurements of ONSD beyond the acute phase of cerebral haemorrhage [8].

The central retinal artery and vein run parallel inside the dura mater of the optic nerve [9] and they are accessible to ultrasound through the identical transorbital acoustic window also used for the ONSD evaluation. Considering their path, we speculate that the ONSD enlargement during raised ICP could be transmitted into the intra-axial structures of the meningeal sheaths and therefore determine flow variations on Doppler parameters of retinal vessels. In this context, very few data are available concerning possible haemodynamic flow alterations of orbital vessels in conditions of elevated ICP, especially for central retinal artery and vein [10,11].

Thus, the primary aim of our study was to evaluate the diagnostic accuracy of OSND values compared with Doppler parameters of retinal vessels for the detection of elevated ICP in acute ICH. The secondary aim was to establish the usefulness of a second assessment of ONSD and Doppler variables of retinal vessels versus CT parameters in acute follow-up of ICH.

Material and methods

Study design and participants

This observational study was performed from January to December 2017 at the "Maggiore della Carità University Hospital" of Novara, Italy. All first-ever spontaneous supratentorial ICH patients admitted to the Neurology and Stroke Unit Department were consecutively enrolled.

Inclusion criteria were: age $\geq$ 18 years old and primary ICH on cerebral CT scan (treated with medical therapies); exclusion criteria were: age < 18 years old, ocular trauma or other conditions that contraindicates ultrasound examination (e.g. glaucoma, orbital tumours), other concomitant causes of intracranial hypertension (e.g. subarachnoid haemorrhage), presence of cardiac arrhythmias that could alter Doppler findings (e.g. atrial fibrillation).

Based on cerebral CT scan findings and clinical conditions, patients with ICH were assigned to the increased ICP group (G1, n=25) and the not increased ICP group (G2, n=21). The control group (n=40) consisted of patients who acceded to the neurosonology laboratory for a Doppler ultrasound assessment of cervical arteries in primary prevention, without ocular pathology and who had never been subjected to lumbar puncture in the past. Each participant underwent general medical, ophthalmologic, and neurological examinations.

For the haemorrhagic patients, radiological evaluation was performed at admission and repeated during their hospital stay, depending on clinical conditions, while sonographic assessment was executed immediately after both cerebral CT scans. Healthy subjects underwent only one sonographic study.

The study was approved by the local ethics committee (Novara No. CE 95/17). All procedures were in accordance with the ethical standards of the responsible committee on human experimentation

(institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Written informed consent was obtained from each participant or legal guardian.

Radiological evaluation

Cerebral CT scans were performed on a Philips, Brillance with 16 rows of detectors, 3 mm of thickness. According to previous studies [12], radiological indicators of raised ICP were defined as follows: midline shift ≥3 mm, compression of cisterns, effacement of sulci with evidence of substantial oedema, collapsed 3rd ventricle, hydrocephalus.

Radiological parameters were contextually recorded. Haemorrhage volume was calculated with the ABC/2 score if rounded or ellipsoid shape [13], while the ABC/3 score was applied if irregular or multinodular [14]. Midline shift was measured as the perpendicular distance between the septum pellucidum and the falx cerebri. An expert neuroradiologist (S.A.), who was unaware about the patients' clinical conditions, independently evaluated the images. The second CT scan was performed over time depending on clinical evolution.

Transorbital sonography

The ultrasonographic studies of ONSD and Doppler indices of retinal vessels were executed with a Toshiba Medical System Aplio 300 (Nasu, Japan) using a high resolution 7.5-11 MHz linear probe with a lateral resolution of <0.4 mm; mechanical index was reduced to <0.2 following ALARA principle [15]. ONSD examinations were performed according to a previously described protocol. In order to perform the ocular ultrasound examination the patients lay in supine position with head elevated to 30°; a large amount of water soluble gel was carefully applied on both the closed upper eyelid and the probe, which was placed on the temporal region of the eye and the optic nerve was detected posterior the globe. Once recognized, 3 measurements (taken 3 mm behind the globe) of the ONSD on the transverse plane were recorded for each eye. By averaging these values, the binocular median ONSD values were obtained for each eye.

The central retinal artery and vein were identified in combination inside the optic nerve using colour Doppler sonography with a low pulse repetition frequency. Angle flow correction was applied, varying between 0 and 45° [16]; gate size was 1.5 mm. At least three complete Doppler waveforms were registered to decrease the effects of physiologic variation [17] and measurements were made approximately at 3 mm behind the globe. From central retinal artery, binocular values of peak systolic velocity (PSV), end diastolic velocity (EDV), and resistive index (RI) were recorded, while maximum and minimum velocity (v-max, v-min) as well as retinal venous pulsation (RVP) were registered from central retinal vein. The averaging of these measurements between the eyes determined the binocular median values of RI and RVP (Figure 1).

ONSD and Doppler imaging were executed directly after CT scan by one single skilled examiner (N.A.), who was accredited by the International Certification in Neurosonology, who was not blinded with regard to the clinical presentation of the patients.

All the measurements were calculated off-line by a second expert neurosonologist (L.P.), blinded to clinical and radiological findings. Agreement between the two operators was preliminarily assessed for ONSD and optic nerve diameter by using the same device in 9 healthy subjects in a previous study [18].

Statistical analysis

Descriptive data are shown as median with interquartile range (IQR) for continuous variables and as numbers and percentages for categorical variables. Differences among three groups were tested using the Kruskal-Wallis test. Radiological and sonographic data between couples of groups were tested using the Wilcoxon-Mann-Whitney test. Diagnostic accuracy in detecting elevated ICP was evaluated using area under the receiver operating characteristic (ROC) curve. Correlation between variables was assessed using the Spearman's coefficient. Statistical analyses were conducted using Stata 13.0/SE (Stata Corp, College Station, TX, USA).

Results

Of the 55 patients who presented with ICH, 9 did not meet the study criteria and were excluded from further analysis (1 glaucoma, 3 did not give any written consent, 2 atrial fibrillation and 3 subarachnoid haemorrhage).

Demographic and clinical data are shown in table 1. Forty-six acute primary ICH patients were recruited, 25 with radiological signs of raised ICP (group 1) and 21 without these signs (group 2); 40 healthy subjects composed the control group. The three groups differed significantly for the median age (lower in group 2) and smoking habits (higher in group 2); no dissimilarities were present for other vascular risk factors. Predictably, patients with increased ICP had higher NIHSS values 28 (IQR 18) at stroke onset than those without 8 (IQR 7).

The main differences in radiological findings and median values of binocular ONSD and Doppler indices among the three groups are presented in table 2. Because of the severity of cerebral haemorrhage within group 1, the radiological control in patients with raised ICP was available for 13 patients (10 patients died, while 2 were lost at follow-up). As expected, the median haemorrhage volume at admission was higher in group 1 with 47.70 cm3 (IQR 47.40) compared to group 2 with 2.20 cm^3 (IQR 0.90) as well as the median midline shift in group 1 with 10.10 mm (IQR 9.60) compared with group 2 with 0.00 mm (IQR 0.00). No significant dissimilarities in ONSD, RI and RVP were observed between patients in group 2 and healthy controls. Median binocular ONSD values in patients with increased ICP were significantly higher from those without at both times of study.

Within group 1, ONSD did not discriminate early mortality risk between patients who died and those who survived (6.63 mm [IQR 0.55] vs. 6.20 mm [IQR 0.45]; p=0.15). Median binocular RI and RVP were significantly higher in patients with raised ICP at both times of assessment, excepting for RVP at control time.

The diagnostic accuracy of sonographic variables in the acute phase of cerebral haemorrhage with their relative cut-off values for the detection of elevated ICP are reported in table 3. ONSD shows the higher accuracy, followed by RI and RVP (ROC curves are compared in figure 2).

Spearman coefficient analysis between radiological and sonographic variables at onset time was statistically significant for ONSD and haemorrhage volume (r=0.677, p=0.0002; figure 3). No significant correlations were documented at control time.

Discussion

To the best of our knowledge, this work provides for the first time information about ocular ultrasound findings of ONSD and Doppler indices of retinal vessels during the acute phase and monitoring of ICH. Our study includes the largest series of ICH patients in this topic and confirms that the ONSD enlarges in the subgroup of ICH patients with elevated ICP.

The main finding of our study is that ONSD shows a higher diagnostic accuracy compared to Doppler indices of central retinal artery and vein for the identification of elevated ICP

Furthermore, the ONSD behaviour in course of elevated ICP is not well established and this is particularly true on ICH patients where only a small case series have been evaluated for this purpose [8]. In this regard, our data show that the widening of the ONSD seems to persist over time in these patients, leading to the hypothesis that ICP is still elevated.

Previous studies showed a positive correlation between ONSD and haemorrhage volume or midline shift [7,8,10]. In patients with ICH and elevated ICP, our work confirmed a good correlation between ONSD and haematoma volume (r=0.677, p=0.0002) at the admission, but missed to find an association with midline shift. A possible explanation of this finding may be due to the elevated age of our patients and the relative brain atrophy that may prevent the early development of cerebral shift. Moreover, midline shift may appear later because of oedema growth. In this regard, our

analysis observed a possible positive trend towards a significant correlation between ONSD and shift values (r=0.40, p=0.17) at control time. Even if speculative, we remark that in group 1 the CT scan and sonographic evaluation were not repeated in 10 subjects because they die. In these patients, an increment of midline shift was conceivable and may have altered the result of a possible significant correlation.

ONSD was not more related to haematoma volume at the time of second CT scan: the reasons may include the initial adsorption of parenchymal blood with no correspondent changes of the ONSD and the drop out of died patients The ONSD thickening seems to follow the variations of raised ICP in chronic conditions like primary intracranial hypertension [19], where the dilatation or contraction of the sheath proceeds slowly. At contrary (if not promptly treated), an acute distension may not be followed by a shrink during ICH, where rapid changes of ICP occur, as observed in subarachnoid haemorrhage [20]. Overall, the oedema growth may maintain an elevated ICP despite the reduction of the haematoma, resulting in a persistent enlargement of ONSD.

The combination of these findings may suggest that variations of ICP could be predicted by serial ONSD evaluations and thus furnish indirect data when compared to radiological signs of elevated ICP; therefore, ultrasound monitoring may give the opportunity to detect and track changes of ICP, providing useful information to optimize treatments in ICH patients [21].

In this context, the attention is currently moving on the possible role of the method in the monitoring of raised ICP during acute conditions, where still little is known. Toscano et al. recently demonstrated the efficacy of the technique for the early identification of malignant increased ICP and brain death in neurocritical patients with ONSD daily monitoring, in order to detect potential candidates for organ donation [22]. In head injury patients, the trend observed in ONSD values obtained by serial measurements provided useful information on decision making, more than the single evaluation [23].

In addition to ONSD ultrasonography, transcranial Doppler sonography with blood velocity studies has been proposed as another alternative non-invasive tool for raised ICP detection [24]. Whether those techniques are promising, data on diagnostic accuracy are variable and no consensus has been reached [25–27]. Recently, the diagnostic performance of Doppler indices of ophthalmic arteries has been compared to ONSD, resulting in lower ability in the detection of elevated ICP. The central retinal artery and vein run parallel inside the optic nerve and they are accessible in their terminal portion through the transorbital window; to best of our knowledge, they have never been studied for this purpose during acute raised ICP. In our hypothesis, the demonstrated maximum enlargement of the ONSD (approximately 3 mm behind the globe) could be transferred to the inward structures and, thus, cause variations on Doppler indices of these vessels. Our findings confirmed this assumption, but results are still limited because of inferiority if compared to the accuracy of ONSD measurements. These results agree with those achieved by Tarzamni, suggesting that the study of the orbital vessels appears to be not accurate enough for the evaluation of ICP because many factors may influence the local flow, including arterial pressure, diseases affecting the small vessels, age of patients, local autoregulation, cerebral perfusion pressure, and inter-individual variability [10].

Finally despite the increasing number of works in this field, there is still no consensus on a unique ONSD cut-off value for the identification of elevated ICP, placed between 4.5 and 6.3 mm [3,5,23]. These discrepancies may depend on various factors, including the execution technique, the subject selection, the underlying pathology and ethnicity, limiting the validation of the method for a more extensive use. Our optimal cut-off point for detection of raised ICP was 5.6 mm, being in line with cited previous reports and more recent findings [28,29].

This study presents some limitations; first at all the small study population. Secondly, we presumed that ICP was normal in control subjects, but we did not perform a CSF opening pressure evaluation. Third, we are aware of the limited predictive value of abnormal CT findings in the assessment of ICP [30]. Finally, the second CT scan was performed not on a given day, but depending on clinical conditions.

Conclusion

The results of this study suggest a higher accuracy of the median binocular ONSD compared to the retinal vessels' Doppler indices in detecting raised ICP. In ICH patients, a second assessment of ONSD measurements may provide other indirect information on persistency of elevated ICP and variations of radiological parameters, but more extensive data are required to confirm this scenario.

References

1 Chen S, Zhao B, Wang W, Shi L, Reis C, Zhang J: Predictors of hematoma expansion predictors after intracerebral hemorrhage. Oncotarget 2017;8:89348–89363.
2 Al-Mufti F, Thabet AM, Singh T, El-Ghanem M, Amuluru K, Gandhi CD: Clinical and radiographic predictors of intracerebral hemorrhage outcome. Interv Neurol 2018;7:118–136.
3 Messerer M, Berhouma M, Messerer R, Dubourg J: [Interest of optic nerve sheath diameter ultrasonography in dectecting non-invasively raised intracranial pressure]. Neurochirurgie 2013;59:55–59.
4 Ohle R, McIsaac SM, Woo MY, Perry JJ: Sonography of the optic nerve sheath diameter for detection of raised intracranial pressure compared to computer tomography: a systematic review and meta-analysis. J Ultrasound Med 2015;34:1285–1294.
5 Dubourg J, Javouhey E, Geeraerts T, Messerer M, Kassai B: Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: a systematic review and meta-analysis. Intensive Care Med 2011;37:1059–1068.
6 Moretti R, Pizzi B, Cassini F, Vivaldi N: Reliability of optic nerve ultrasound for the evaluation of patients with spontaneous intracranial hemorrhage. Neurocrit Care 2009;11:406–410.
7 Školoudík D, Herzig R, Fadrná T, Bar M, Hradílek P, Roubec M, Jelínková M, Šaňák D, Král M, Chmelová J, Heřman M, Langová K, Kaňovský P: Distal enlargement of the optic nerve sheath in the hyperacute stage of intracerebral haemorrhage. Br J Ophthalmol 2011;95:217–221.
8 Lochner P, Mader C, Nardone R, Tezzon F, Zedde ML, Malferrari G, Brigo F: Sonography of the optic nerve sheath beyond the hyperacute stage of intracerebral hemorrhage. J Ultrasound 2014;17:225–228.
9 Bird B, Stawicki SP: Anatomy, Head, Face, Eye, Arteries, Ophthalmic. 2017 Dec 29. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-. Available from http://www.ncbi.nlm.nih.gov/books/NBK482317/ PubMed PMID: 29493942.
10 Tarzamni MK, Derakhshan B, Meshkini A, Merat H, Fouladi DF, Mostafazadeh S, Rezakhah A: The diagnostic performance of ultrasonographic optic nerve sheath diameter and color Doppler indices of the ophthalmic arteries in detecting elevated intracranial pressure. Clin Neurol Neurosurg 2016;141:82–88.
11 Querfurth HW, Lagrèze WD Hedges TR 3rd, Heggerick PA: Flow velocity and pulsatility of the ocular circulation in chronic intracranial hypertension. Acta Neurol Scand 2002:105:431–440.
12 Eisenberg HM, Gary HE Jr, Aldrich EF, Saydjari C, Turner B, Foulkes MA, Jane JA, Marmarou A, Marshall LF, Young HF: Initial CT findings in 753 patients with severe head injury. A report from the NIH Traumatic Coma Data Bank. J Neurosurg 1990;73:688–698.
13 Kothari RU, Brott T, Broderick JP, Barsan WG, Sauerbeck LR, Zuccarello M, Khoury J: The ABCs of measuring intracerebral hemorrhage volumes. Stroke 1996;27:1304–1305.
14 Huttner HB, Steiner T, Hartmann M, Köhrmann M, Juettler E, Mueller S, Wikner J, Meyding-Lamade U, Schramm P, Schwab S, Schellinger PD: Comparison of ABC/2 estimation technique to computer-assisted planimetric analysis in warfarin-related intracerebral parenchymal hemorrhage. Stroke 2006;37:404–408.
15 Ertl M, Gamulescu MA, Schlachetzki F (2012). Application of Orbital Sonography in Neurology, Sonography, Dr. Kerry Thoirs (Ed.). Sonography, Dr. Kerry Thoirs (Ed.), ISBN: 978-953-307-947-9, InTech, Available from: http://www.intechopen.com/books/sonography/application-of-orbital-sonography-in-neurology
16 Baxter GM, Williamson TH: Color Doppler imaging of the eye: normal ranges, reproducibility, and observer variation. J Ultrasound Med 1995;14:91–96.

17 Williamson TH, Harris A: Color Doppler ultrasound imaging of the eye and orbit. Surv Ophthalmol 1996;40:255–267.
18 Lochner P, Cantello R, Brigo F, Coppo L, Nardone R, Tezzon F, Raymkulova O, Strigaro G, Comi C, Leone MA: Transorbital sonography in acute optic neuritis: a case-control study. AJNR Am J Neuroradiol 2014;35:2371–2375.
19 Lochner P, Fassbender K, Lesmeister M, Nardone R, Orioli A, Brigo F, Stolz E: Ocular ultrasound for monitoring pseudotumor cerebri syndrome. J Neurol 2018;265:356–361.
20 Bäuerle J, Niesen WD, Egger K, Buttler KJ, Reinhard M: Enlarged Optic Nerve Sheath in Aneurysmal Subarachnoid Hemorrhage despite Normal Intracranial Pressure. J Neuroimaging 2016;26:194–196.
21 Robba C, Bacigaluppi S, Cardim D, Donnelly J, Bertuccio A, Czosnyka M: Non-invasive assessment of intracranial pressure. Acta Neurol Scand 2016;134:4–21.
22 Toscano M, Spadetta G, Pulitano P, Rocco M, Di Piero V, Mecarelli O, Vicenzini E: Optic nerve sheath diameter ultrasound evaluation in intensive care unit: possible role and clinical aspects in neurological critical patients' daily monitoring. Biomed Res Int 2017;2017:1621428.
23 Thotakura AK, Marabathina NR, Danaboyina AR, Mareddy RR: Role of serial ultrasonic optic nerve sheath diameter monitoring in head injury. Neurochirurgie 2017;63:444–448.
24 Hassler W, Steinmetz H, Gawlowski J: Transcranial Doppler ultrasonography in raised intracranial pressure and in intracranial circulatory arrest. J Neurosurg 1988;68:745–751.
25 Nair S: Clinical review of non-invasive intracranial pressure measurement in medical cases. J Neuroanaesthesiol Crit Care 2016;3:9–14.
26 Morgalla MH, Magunia H: Noninvasive measurement of intracranial pressure via the pulsatility index on transcranial Doppler sonography: Is improvement possible? J Clin Ultrasound 2016;44:40–45.
27 Cardim D, Robba C, Bohdanowicz M, Donnelly J, Cabella B, Liu X, Cabeleira M, Smielewski P, Schmidt B, Czosnyka M: Non-invasive Monitoring of Intracranial Pressure Using Transcranial Doppler Ultrasonography: Is It Possible? Neurocrit Care 2016;25:473–491.
28 Lee SU, Jeon JP, Lee H, Han JH, Seo M, Byoun HS, Cho WS, Ryu HG, Kang HS, Kim JE, Kim HC, Jang KS: Optic nerve sheath diameter threshold by ocular ultrasonography for detection of increased intracranial pressure in Korean adult patients with brain lesions. Medicine (Baltimore) 2016;95:e5061.
29 Amini A, Kariman H, Arhami Dolatabadi A, Hatamabadi HR, Derakhshanfar H, Mansouri B, Safari S, Eqtesadi R: Use of the sonographic diameter of optic nerve sheath to estimate intracranial pressure. Am J Emerg Med 2013;31:236–239.
30 Rosenberg JB, Shiloh AL, Savel RH, Eisen LA: Non-invasive methods of estimating intracranial pressure. Neurocrit Care 2011;15:599–608.

Table 1. Demographic and clinical data

Characteristic	Cerebral haemorrhage		Healthy Controls (n = 40)	p-Value
	With increased ICP (n = 25)	Without increased ICP (n = 21)		
Age years (median, IQR)	80 (14)	72 (13)	77 (12)	0.01
Male sex (n, %)	11 (44)	14 (67)	21 (53)	NS
Arterial hypertension (n, %)	21 (84)	16 (76)	30 (75)	NS
Diabetes (n, %)	5 (20)	9 (43)	6 (15)	NS
Dyslipidaemia (n, %)	12 (48)	11 (52)	22 (55)	NS
History of heart disease (n, %)	6 (24)	4 (19)	6 (15)	NS
Smoke (n, %)	4 (16)	9 (43)	6 (15)	0.05
NIHSS at onset (median, IQR)	28 (18)	8 (7)	-	<0.001

IQR: interquartile range; NIHSS: National Institutes of Health Stroke Scale; $p<0.05$ was considered statistically significant.

Table 2. Radiological and sonographic data in patients with cerebral haemorrhage and controls.

Variable	**Cerebral haemorrhage**				
At admission	**With increased ICP (G1) (n = 25)**	***p-Value G1/G2***	**Without increased ICP (G2) (n = 21)**	***p-Value G2/Controls***	**Healthy Controls n = 40**
ONSD (mm)	6.40 (0.60)	<0.01	4.70 (0.40)	NS	4.50 (0.25)
RI	0.79 (0.11)	0.01	0.77 (0.03)	NS	0.75 (0.07)
RVP (cm/s)	3.20 (1.05)	0.02	2.00 (1.55)	NS	2.30 (0.68)
Haemorrhage volume (cm^3)	47.70 (47.40)	<0.01	2.20 (0.90)	-	-
Midline Shift (mm)	10.10 (9.60)	<0.01	0.00 (0.00)	-	-
At control time	**(n = 13)**		**(n = 21)**		
ONSD (mm)	6.00 (0.60)	<0.01	4.55 (0.40)	-	-
RI	0.80 (0.06)	0.01	0.75 (0.35)	-	-
RVP (cm/s)	2.80 (1.25)	NS	2.40 (1.40)	-	-
Haemorrhage volume (cm^3)	45.00 (38.70)	<0.01	2.00 (1.60)	-	-
Midline Shift (mm)	8.80 (6.10)	<0.01	0.00 (0.00)	-	-
Time of CT control (days)	3 (2)	NS 0.21	5 (5)	-	-

Sonographic data are intended as binocular values; all data are expressed as median (interquartile range, IQR). ONSD: optic nerve sheath diameter; RI: resistive index; RVP: retinal venous pulsation; NS: not significant. $p<0.05$ was considered statistically significant.

Table 3. Diagnostic accuracy and relative cut-off values of the single variables for the detection of raised ICP

Parameter	AUC	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)
ONSD	1.00	1.00 – 1.00	5.60	100	100
RI	0.72	0.58 – 0.87	0.80	48	95
RVP	0.70	0.54 – 0.86	2.73	80	62

AUC: area under the curve; CI: confidence interval; ONSD: optic nerve sheath diameter; RI: resistivity index; RVP: retinal venous pulsation.

Fig. 1. Representation of main ocular sonographic (optic nerve sheath diameter, ONSD; resistive index, RI; retinal venous pulsation, RVP) and radiological findings (brain CT scan) in ICH patients with (left) and without (right) elevated ICP.

Fig. 2. Comparison of receiver operator characteristic (ROC) curves for the identification of elevated ICP among the variables (ONSD, optic nerve sheath diameter; RI, resistive index; RVP, retinal venous pulsation).

Fig. 3. Spearman correlation between median binocular ONSD (mm) and haematoma volume (cm3) at onset of cerebral haemorrhage in patients of group 1.

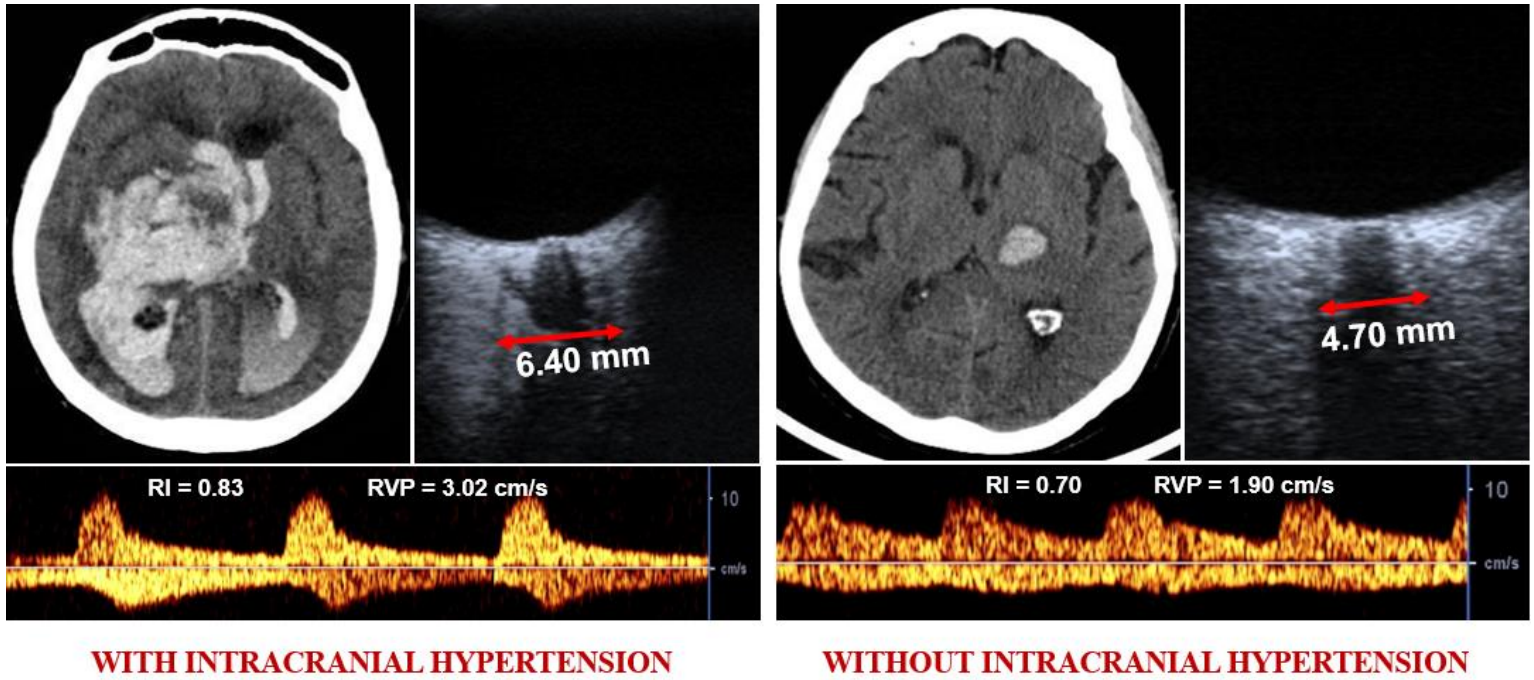

Fig. 1. Representation of main ocular sonographic (optic nerve sheath diameter, ONSD; resistive index, RI; retinal venous pulsation, RVP) and radiological findings (brain CT scan) in ICH patients with (left) and without (right) elevated ICP.

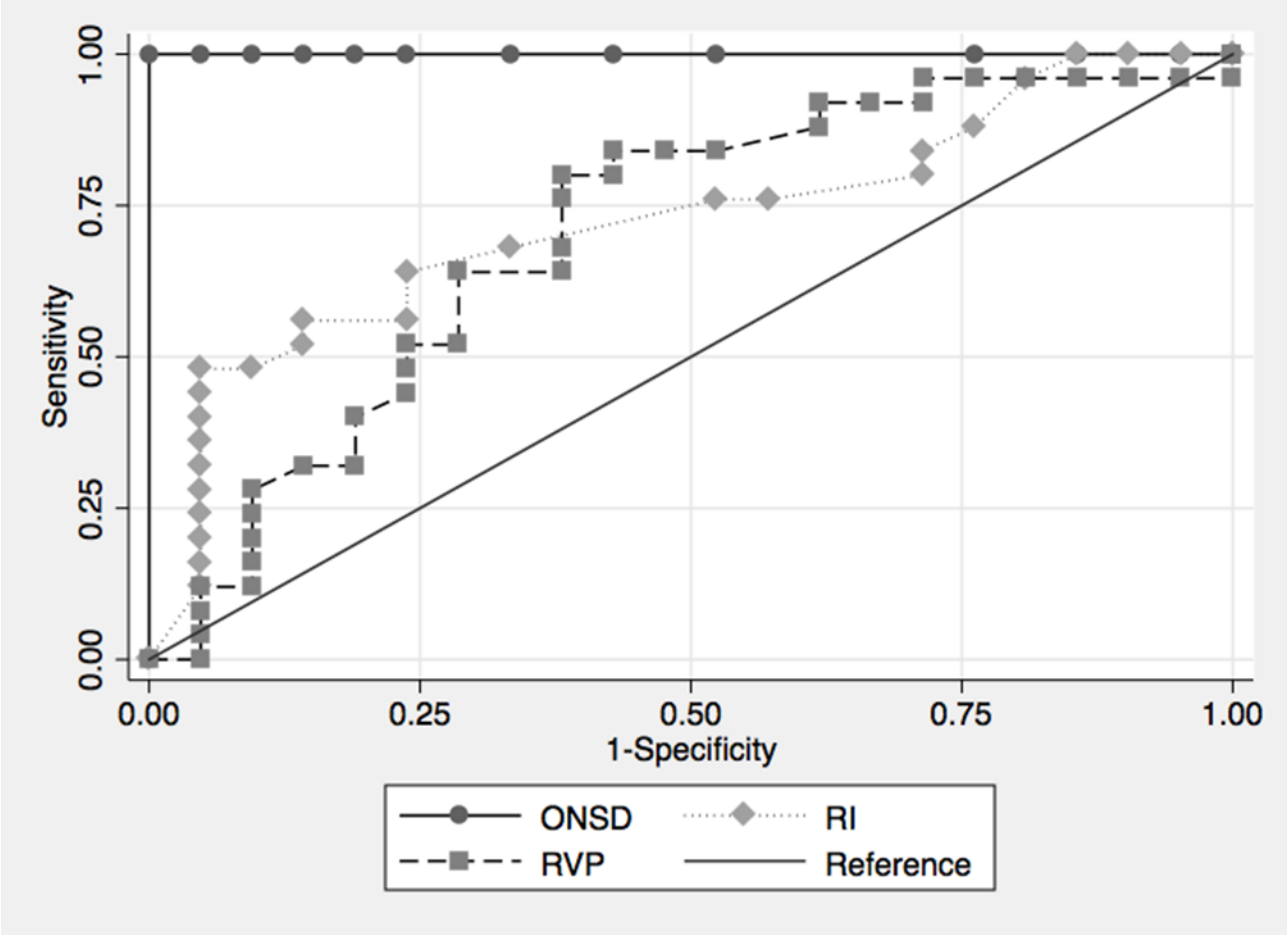

Fig. 2. Comparison of receiver operator characteristic (ROC) curves for the identification of elevated ICP among the variables (ONSD, optic nerve sheath diameter; RI, resistive index; RVP, retinal venous pulsation).

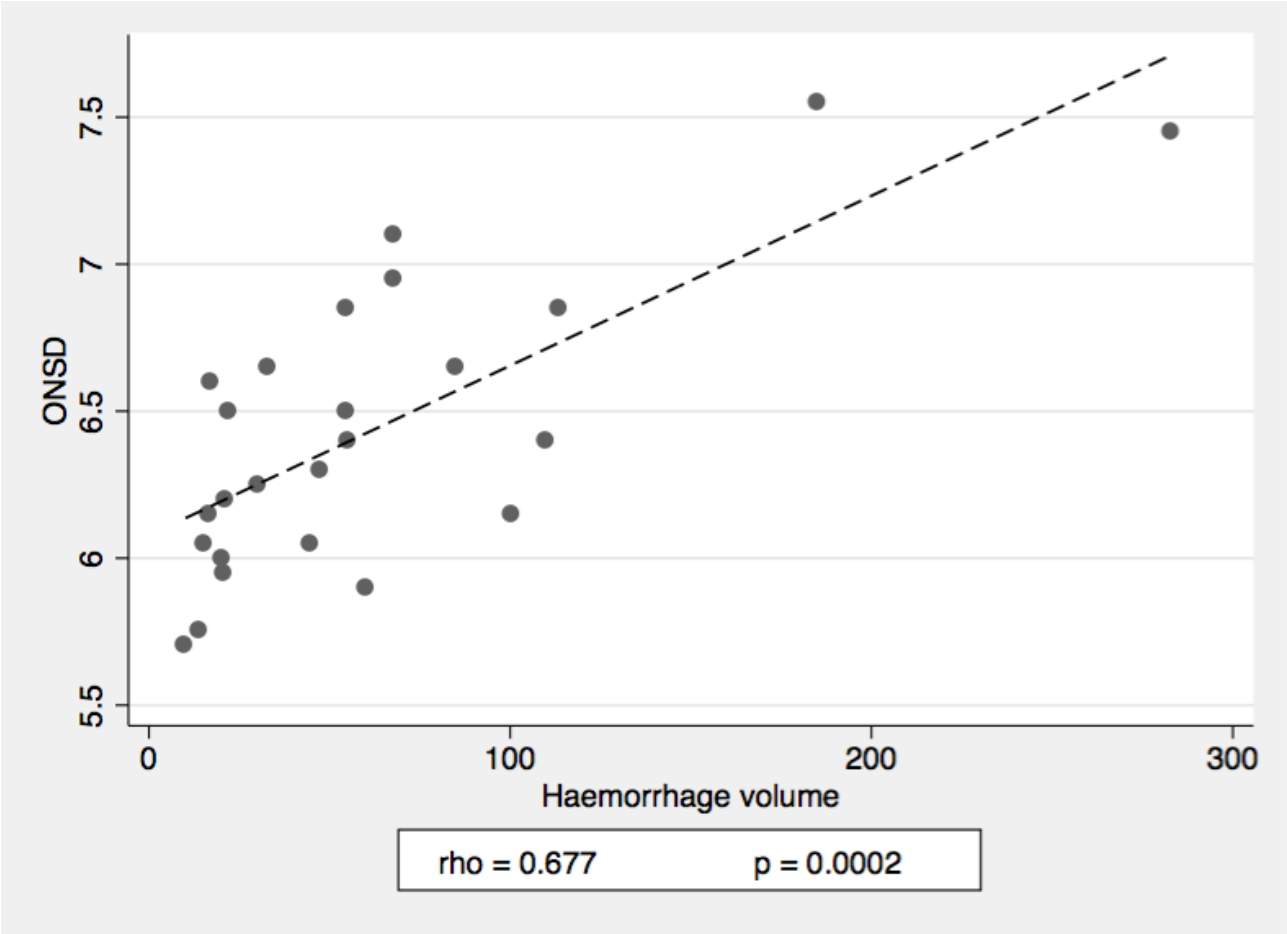

Fig. 3. Spearman correlation between median binocular ONSD (mm) and haematoma volume (cm^3) at onset of cerebral haemorrhage in patients of group G1