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Correlation between the Optic Nerve Sheath Diameter Measurement and Intracranial Hypertension Tomographic Findings from a Colombian Hospital

Correlação entre a medição do diâmetro da bainha do nervo óptico e os achados tomográficos da hipertensão intracraniana em um hospital colombiano

Andrés Fabricio Caballero-Lozada[1,2,3,4] Jorge Fernando Miño-Bernal[2]
Rene Alberto Espinosa-Marsiglia[1,2] Valentina Rojas-Rincón[4]

[1] Department of Anesthesiology and Resuscitation, Universidad del Valle, Cali, Colombia
[2] Department of Anesthesiology, Hospital Universitario del Valle, Cali, Colombia
[3] Fundación Hospital San José de Buga, Buga, Colombia
[4] Department of Anesthesiology, Unidad Central del Valle del Cauca, Tuluá, Colombia

Address for correspondence Andrés Fabricio Caballero-Lozada, MD, Department of Anesthesiology and resuscitation. Universidad del Valle, Street 4B # 36-00, Cali, Colombia (e-mail: andres.caballero@correounivalle.edu.co).

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Abstract

Objective In the present study, we aimed at determining the correlation between tomographic findings of intracranial hypertension and ultrasound measurement of the optic nerve sheath diameter (ONSD).

Methods Observational, descriptive, prospective, cross-sectional pilot study. The present research was performed in a tertiary hospital in Cali, Colombia, from March 2019 to October 2019. Twenty-five patients constituted the intracranial hypertension group, and 25 patients without intracranial hypertension constituted the control group. Ultrasound measurements of the ONSD were assessed using a Sonosite Turbo (SonoSite Inc., Bothell, WA, USA) ultrasound. The computed tomography (CT) images obtained from each patient diagnosed with intracranial hypertension were available in the software of the hospital. The primary outcome was the ultrasound measurement of the ONSD.

Results The ONSD values of the right eye of the intracranial hypertension group ranged from 5.2 to 7.6 mm, and the ONSD of the left eye ranged from 5.3 to 7.3 mm. The global ONSD values, obtained from the average between the right and left eye, were recorded between 5.25 and 7.45 mm. Overall, our study indicated that ultrasound measurements of the ONSD were effective in differentiating a group with intracranial hypertension, previously diagnosed by CT scan images, from patients

Keywords

- ► Optic nerve
- ► Intracranial hypertension
- ► Ultrasonography
- ► Tomography, X-Ray Computed

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without this condition. According to the ROC curve, the optimal cutoff point for detecting intracranial hypertension was 5.2 mm.

Conclusions Ultrasound measurements of the ONSD correlated with the measurements obtained from CT scan images, suggesting that the ultrasound technique can be efficient in identifying patients with intracranial hypertension and valuable in cases when CT scan images are not an available option.

Resumo

Objetivo No presente estudo, pretendemos determinar a correlação entre os achados tomográficos da hipertensão intracraniana e a medida ultrassonográfica do diâmetro da bainha do nervo óptico (DBNO).

Métodos Estudo piloto, observacional, descritivo, prospectivo e transversal. A presente pesquisa foi realizada em um hospital terciário de Cali, na Colômbia, de março de 2019 a outubro de 2019. Vinte e cinco pacientes fizeram parte do grupo de hipertensão intracraniana e 25 pacientes sem hipertensão intracraniana fizeram parte do grupo controle. O ultrassom Sonosite Turbo (SonoSite Inc., Bothell, WA, EUA) foi utilizado para a medição ultrassonográfica do DBNO. As imagens tomográficas computadorizadas obtidas de cada paciente com diagnóstico de hipertensão intracraniana estavam disponíveis no software do Hospital. O resultado primário foi a medida ultrassonográfica do DBNO.

Resultados Os valores de DBNO do olho direito do grupo de hipertensão intracraniana foram de 5,2 a 7,6 mm e o DBNO do olho esquerdo foi de 5,3 a 7,3 mm. No que se refere aos valores globais de DBNO obtidos a partir da média entre o olho direito e o olho esquerdo, registrou-se entre 5,25 e 7,45mm. No geral, o presente estudo indicou que as medições ultrassonográficas do DBNO foram eficazes na diferenciação de um grupo com hipertensão intracraniana, previamente diagnosticada por imagens de tomografia computadorizada (TC), de pacientes sem essa condição. De acordo com a curva ROC, o ponto de corte ideal para detectar hipertensão intracraniana foi de 5,2 mm.

Conclusões De acordo com nossos achados, as medidas ultrassonográficas do ONSD se correlacionaram com as medidas obtidas nas imagens de TC, sugerindo que a técnica ultrassonográfica pode ser eficiente para identificar pacientes com hipertensão intracraniana e útil nos casos em que as imagens tomográficas não são uma opção disponível.

Palavras-chave
- ► Nervo Óptico
- ► Hipertensão Intracraniana
- ► Ultrassonografia
- ► Tomografia Computadorizada por Raios X

Introduction

Patients with neurological conditions make up 15% of admissions to the intensive care unit (ICU), where the management of cerebral edema, intracranial hypertension, vasospasm, and epileptic status is frequent.[1] The definition of intracranial hypertension is an intracranial pressure (ICP) $>$ 20 mm Hg for $>$ 5 minutes. It is a catastrophic neurological event associated with a poor prognosis for the life and functionality of the patient regardless of its etiology.[2] According to the clinical practice guidelines, the management of this condition must be done early and aggressively. Increased ICP reduces cerebral perfusion pressure, exacerbating a secondary brain injury jointly with ischemia and a fatal clinical prognosis.[3]

Clinically, this pathology manifests nonspecifically, and the use of computed tomography (CT) of the skull is necessary to document the displacement of vascular and parenchymal structures. Unfortunately, the availability of a CT scanner in specific regions or at certain times of the day is limited. Additionally, there is also a delay in taking the CT, which influences the neurological prognosis under the premise that "time is brain." Thus, the question arises: Is there a fast, noninvasive, accessible, and bedside method that can guide a diagnosis of intracranial hypertension? The answer would be with the ultrasound (US). In this context, our purpose was to determine the correlation between tomographic findings of intracranial hypertension and US measurement of the optic nerve sheath diameter (ONSD).

Materials and Methods

Study Design

This was an observational, descriptive, prospective, cross-sectional pilot study.

Setting

The present study was conducted from March 11, 2019 to October 27, 2019 at the Hospital Universitario del Valle (Cali, Colombia). Confidentiality of patients and control individuals was guaranteed; a unique alphanumeric code identified each participant. All participants gave informed consent.

Participants

A convenience sample of 25 patients constituted the intracranial hypertension group, and 25 patients without intracranial hypertension constituted the control group. The inclusion criteria were patients with clinical and tomographic signs of intracranial hypertension, without previous neurological pathology, admitted to the Emergency Department and to the ICU of the Hospital Universitario del Valle (Cali, Colombia), and with recent tomography < 24 hours at the time of measurement. The exclusion criteria were patients <18 years old with chronic neurological deterioration, basic ophthalmological comorbidities, optic neuritis, and/or ocular trauma. Likewise, outpatients with arachnoid cyst, lesions that compromise the cavernous sinus without good pain management, and operating difficulties in performing the procedure were excluded. Patients who withdrew after signing the informed consent or reported pain when performing the procedure were removed from the study.

Variables

The variables evaluated included US measurement of the global ONSD and the ONSD for the right and left eye, gender, age, pupil reactivity, intracranial hypertension condition, surgical management, tomographic findings, and successful intracranial hypertension diagnosis with US measurement of the ONSD.

Data Sources/Measurement

For data collection, a tabulated data collection format was designed in IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA). The format included the variables to be evaluated. The ONSD was measured with the Sonosite Turbo ultrasound scanner (SonoSite Inc., Bothell, WA, USA), using a 13 to 6 MHz linear transducer (►**Fig. 1**). During the procedure, the participants were in a relaxed supine position. The procedure was based on the proposals made by Ohle et al.[4] and by Moretti et al.[5] The US equipment was placed in front of the operator, and the US gel was applied on the upper eyelid, obtaining an image of the optic nerve in the

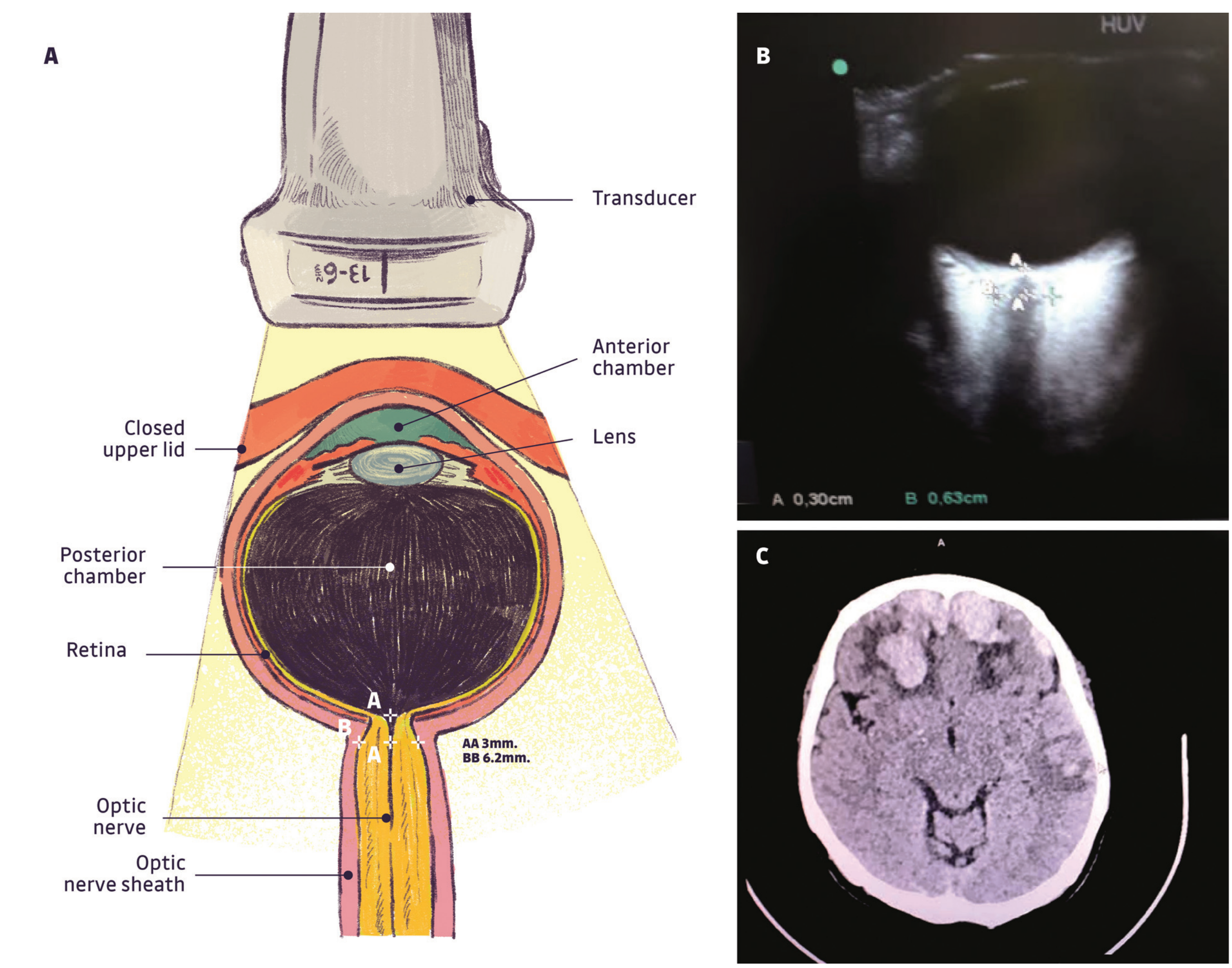

Fig. 1 (A) Illustration of ONSD measurement using the SONOSITE TURBO ultrasound scanner. (B) Ultrasonographic image of the optic nerve. (C) Tomographic image of the optic nerve.

axial plane. The ONSD measurements were performed at a depth of three behind the orbit, and three measurements were performed for each eye. The duration of the procedure was 5 minutes.

To compare the previous measurement with the tomographic images obtained from each patient, the information available in the "Integra" system was obtained. This information was part of the Hospital Universitario del Valle software for patients with symptoms of intracranial hypertension corroborated by previously mentioned tomographic findings.

Statistical Methods

A paired *t*-test was performed for independent samples (95% confidence intervals [CIs]), evaluating the distribution of the ONSD value in patients with intracranial hypertension versus the distribution of the ONSD value in the control population. In addition, a Pearson R correlation was performed between left and right ONSDs, looking to see if it is affected by the presence of anisocoria or by the spatial location of the lesion. The ONSD and age and ONSD and gender correlations were performed to assess whether the ONSD varies between the different age groups or if there are significant differences between genders. Also, it was studied if there are differences in the ONSD measurement between patients with intracranial hypertension undergoing surgical or conservative management.

The tomographic findings were used to identify signs of intracranial hypertension and were classified according to deviation from the midline, absence of cortical-subcortical differentiation, effacement of grooves, and ventricular megaly. Each of these variables was assigned a score of 1, and its sum was correlated with the ONSD value.

Several authors establish different cutoff points for the ONSD from 4.85 mm to 6.3 mm,[6,7] so it was defined by consensus a cutoff point of 5.5 mm.[8] This value was used to detect intracranial hypertension and represented a change in the CT images. This cutoff point defines the presence or absence of intracranial hypertension; a 2×2 test was performed among the population of cases and controls, looking for the sensitivity and specificity of this value in the study population. In this way, the likelihood ratio was defined, the probability of diagnosing intracranial hypertension using the ONSD measurement. Later, these data were unified in a ROC curve as a global and independent measure of the cutoff point.

Results

The data collection was performed between March 11 and October 27, 2019, at the Hospital Universitario del Valle. We recruited 50 individuals, of which 25 were patients with intracranial hypertension, and 25 individuals with no clinical history of intracranial hypertension were used as a control population. Of the intracranial hypertension group, 19 were men (76%), and the age varied between 19 and 82 years old. However, the most common age range was from 55 to 64 years old (28%). Of the control group, 16 subjects were men (64%), and the age varied between 18 and 72 years old; however, the most common age range was from 18 to 27 years old (40%).

Regarding surgical management, 18 (72%) patients with intracranial hypertension required decompressive neurosurgical management. The tomographic finding that suggested intracranial hypertension was the midline deviation, ventricular dilation compatible with hydrocephalus, effacement of the corticosubcortical relationship, and effacement of the grooves. A total of 2 tomographic findings were found in 12 (48%) patients, 1 finding in 6 (24%) patients, 3 findings in 5 (20%) patients, and 4 findings in 2 (8%) patients. A total of 22 (88%) patients presented reactive pupils. In the control group, the pupils of the 25 control individuals were reactive.

In the mean difference test of the ONSD values of the patients with hypertension, there were no significant differences between the measurements of both eyes ($p = 0.43$; 95% CI: - 0.16–0.36). Likewise, in the test for the mean difference of the ONSD values of the control individuals, there were no significant differences between the measurements of both eyes ($p = 0.89$; 95%CI: - 0.26–0.23). To compare the ONSD values of both groups, a paired *t*-test for independent samples was performed. Normality was first tested with the Shapiro-Wilk test, and homogeneity of variance with the Levene test for both groups. The paired test showed that there were significant differences between the means ($p < 0.05$; 95%CI: 1.31469–1.77331) (►**Table 1**).

In the Pearson correlation analysis between the ONSD of the right eye and the ONSD of the left eye of patients with intracranial hypertension, a coefficient of 0.68 was found, indicating a positive correlation (95%CI: 0.3816268–0.8447966). As for the control individuals, the average values of the right ONSD and the left ONSD correlated 0.58 (95%CI: 0.2333799–0.7907734). The correlation between the global ONSD values of patients with intracranial hypertension with age was - 0.20, indicating that the variables are inversely related (95%CI: - 0.5522713–0.2108760). For control individuals, a positive correlation of 0.29 between global ONSD values and age was found. Also, the correlation coefficient between the global ONSD values in patients with intracranial hypertension and the number of findings was 0.68 (95%CI: 0.3928022–0.8485192), indicating a positive correlation.

According to the results, of the 25 patients with intracranial hypertension diagnosed with CT, 24 were successfully

Table 1 Optic nerve sheath diameter values for the right and left eyes of the intracranial hypertension group and the control group

	ONSD (mm)			*p-value*
	Right eye	Left eye	Global	
Intracranial hypertension group	5.2–7.6	5.3–7.3	5.25–7.45	< 0.05
Control group	3.3–5.5	3.2–5.4	3.25–5.15	

Abbreviation: ONSD, optic nerve sheath diameter.

Table 2 Case-control study

Intracranial hypertension		Group		Total
		Cases	Controls	
	Present	24	0	24
	Absent	1	25	26
	Total	25	25	50

diagnosed with US (►**Table 2**). In addition, it was found that the specificity was high (100%), indicating that the disease will be ruled out when the result of the patient is negative. Likewise, the sensitivity was high (96%), indicating that the presence of the disease will be confirmed when a patient has a positive test result (►**Table 3**). In this case, the positive likelihood ratio, being infinite, is a measure of great magnitude since it allows us to confidently confirm the presence of intracranial hypertension when performing the measurement of ONSD by US. On the other hand, regarding the negative likelihood ratio, the lower it is, the better the study, since it rules out the disease; in this case, its value was 0.04 (►**Table 3**).

Subsequently, the patient data was unified to construct a ROC curve, finding an optimal cutoff point of 5.2 mm (►**Fig. 2**). Since the area under the curve (AUC) was 1, it can be inferred that the US ONSD measurement, used as a diagnostic test to classify patients with cranial hypertension and control patients, is ideal.

Discussion

Overall, the study indicated that US measurements of the ONSD were effective in differentiating a group with intracranial hypertension, previously diagnosed by CT scan images, from patients without this condition. However, as the study is limited by sample size, more studies should be made with a more significant sample to further validate the results. Nevertheless, the results are consistent with the findings of other studies. For instance, Blaivas et al.[9] sought to determine whether optic nerve sheath dilation, as detected

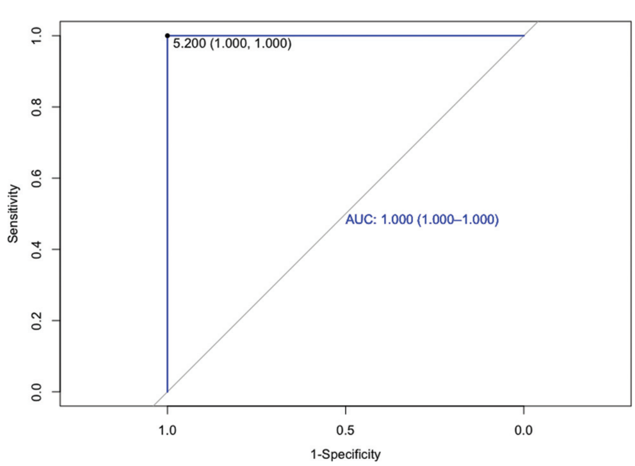

Fig. 2 ROC curve analysis.

Table 3 Characteristics of the case-control study

Characteristic	Value
Cutoff point	5.5mm
Sensitivity	96%
Specificity	100%
Positive likelihood ratio test	Infinite
Negative Likelihood ratio test	0.04
Positive predictive value	96%
Negative predictive value	100%
Area under the curve	Not built

in emergencies by the US with the Agilent Image Point Hx (Phillips, Andover, MA, USA) machine, could be reliably correlated with head CT findings suggesting elevated ICP in acute head injury patients. The authors found that all cases of CT-determined elevated ICP were correctly predicted by ONSD $>$ 5 mm measured with US. The authors found for ONSD a sensitivity of 100% and a specificity of 95% in the measurement with US compared with CT. Likewise, Girisgin et al.[10] performed the ONSD measurement using a 7.5 MHz transducer in 28 patients with intracranial hypertension determined by CT, defined as effacement of the sulci, transfalcin herniation, and changes in the ratio of gray matter and white matter, and a control group of 26 patients without the illness. The average value of the ONSD in patients with intracranial hypertension was 6.4 mm, and 4.6 mm in control patients, finding a statistically significant difference between both groups ($p = 0.001$). The authors concluded that US use in the measurement of ONSD is helpful in the early and rapid detection of intracranial hypertension.

Moreover, Lee et al.[11] performed a multicenter study in which they identified 3 groups of patients, 1 with intracranial hypertension ($n = 81$), another with patients without intracranial hypertension ($n = 27$), and a control group ($n = 26$). The identification of intracranial hypertension, measured with a ProSound Alpha 6 13-MHz US probe (Hitachi Medical Corp., Tokyo, Japan), was extrapolated according to tomographic findings given by diffusion of cerebral sulci, significant cerebral edema, compression of cisterns, displacement of the midline, and absence in the differentiation of gray and white matter. The ONSD was significantly higher in patients with intracranial hypertension (5.9mm [5.8– 6.2]) than in those in the group without intracranial hypertension (5.2mm [4.8–5.4]) and in the control group (4.9mm [4.6–5.2]) ($p < 0.01$). There were no significant differences between patients without intracranial hypertension and the control population ($p = 0.31$). According to their results, the authors contemplated a cutoff point for ONSD of 5.5mm with a sensitivity of 99% (95%CI: 0.93–1.00) and a specificity of 85% (95%CI: 0.66–0.96%).

Ultrasound-guided ONSD measurement and ICP measurement have also been previously studied.[12–14] Cammarata et al.[15] studied 11 patients with severe head trauma admitted to an ICU with a Glasgow coma scale score $<$ 8 points that required management with ICP monitoring. The authors measured ONSD by US with the Model Vivid Expert (General Electric Medical System, Milwaukee, WI) and found that the ONSD values among patients with ICP < 20 mmHg were similar to the values of patients without intracranial pathology. Also, the authors found a significant positive correlation between ONSD and ICP ($r = 0.74$; $p = 0.001$), concluding that ocular US may be considered as a good alternative for a rapid indirect evaluation of ICP in patients with head trauma. Similarly, Frumin et al.[16] evaluated 27 patients in a neurosurgical unit, of which 22% had an ICP > 20 mm Hg. According to the Spearman method, the authors reported a positive correlation between the ONSD measured by US with a SONOSITE M-TURBO (SonoSite Inc., Bothell, WA, USA) and intracranial hypertension AUC of 0.871 (95%CI: 0.67–0.96). Also, the authors recorded that an ONSD > 5.2 mm was a strong predictor of intracranial hypertension with a sensitivity of 83% (95%CI: 0.35–0.99) and a specificity of 100% (95%CI: 0.84–1.00).

Dubourg et al.[17] evaluated 6 studies that included 231 patients characterized by being homogeneous among themselves to compare ICP values with the measurement of the ONSD. The authors found a sensitivity of 90% (95%CI: 0.80–0.95), a specificity of 85% (95%CI: 0.73–0.93), with an AUC of 0.94% (95%CI: 0.91–0.96). With these results, they concluded that there was a correlation between the two variables and suggested using this proper US method in clinical decision-making.

Limitations

The present study has some limitations. First, given the nature of the study design used and the limited sample size, the results require further validation.

Conclusions

According to findings in the multimodal clinical context of the neurocritical patient, US would be a quick and noninvasive tool at the bedside of the patient. Therefore, it is suggested implementing US measurements to improve survival and neurological prognosis, detecting an elevated ICP in cases when CT scan images are not an available option. In addition, US measurements would allow the detection of increasing ICP before deciding an invasive neurosurgical monitoring. According to the ROC curve, the optimal cutoff point for detecting intracranial hypertension was 5.2 mm. Moreover, comparing the study that was made with others, in terms of the US machine used to measure the ONSD, it is likely that the equipment does not influence the effective results found here. Nevertheless, more studies should be made with a more significant sample to further validate the results.

Informed Consent and Patient Details

The authors declare that the present report does not contain any personal information that could identify the patient(s) or volunteers.

Presentation

Preliminary data for the present study were presented as an abstract European Anaesthesiology Congress 2020. European Journal of Anaesthesiology. 2020;37(e-Supplement 58):191

Ethics

The Institutional Committee for the Review of Human Ethics of the Universidad del Valle (Cali, Colombia) on February 28, 2019, gave the ethical approval for the present study (Ethical Committee N° 221–018).

Author Contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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Conflict of Interests

The authors have no conflict of interests to declare.

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