

Optic nerve sheath diameter measured using magnetic resonance imaging and factors that influence results in healthy Chinese adults: a cross-sectional study

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To the Editor: Identifying the increase in intracranial pressure (ICP) is very important in the management of neurosurgical and neurological disorders, because raised ICP is associated with poor outcomes such as brain herniation and death. Although the intraparenchymal or intraventricular invasive methods remain the gold standard for ICP measurement, they cannot be routinely employed because of the lack of an adequate number of neurosurgeons. In addition, because of contraindications (eg, blood coagulation disorders and severe platelet disorders) and complications (eg, infection and hemorrhage), the invasive approach is not always possible.^[1] Therefore, accurate non-invasive methods are needed to estimate ICP in clinical practice. A large number of studies have shown that the optic nerve sheath diameter (ONSD) is an indirect marker of ICP, and that there is a linear relationship between the two parameters.^[1,2] Therefore, ONSD and its accurate measurement methods are getting more and more attention from scholars.

Non-invasive methods such as ultrasound and magnetic resonance imaging (MRI) are becoming increasingly used by researchers to measure ONSD because of their clinical value.^[3,4] However, due to the lack of an anatomical structure and the boundary definition of ultrasound, its accuracy as an ONSD measurement tool remains to be proved. Considering the high spatial resolution and the clear delineation of orbital structures, we applied the time-of-flight (TOF) magnetic resonance angiography (MRA) technique to obtain the images of ONSD; thus it can accurately measure ONSD and provide reliable information on ICP.^[3]

However, since the available data on the value of normal ONSD measured by MRI are inconclusive, it is difficult to define the diagnostic criteria for raised ICP. Therefore, well-established, normal values are needed at the clinical level. Although some studies have measured the normal range of ONSD using MRI, most of them were based on Caucasian participants and contained only a small number of healthy subjects.^[3] Therefore, the aim of the present study was to establish normative values for ONSD using MRI among a large number of healthy Chinese adults. The relationship between ONSD and the demographic, clinical, and anatomical parameters were also evaluated.

The Ethics Committee of the University of Science and Technology of China (USTC) approved this study. Due to the retrospective nature of the study, informed consent was not required.

The current study reviewed the brain MRI scans of 428 participants who underwent a comprehensive physical examination at the First Affiliated Hospital of the USTC between July 2017 and November 2019. To be included, the study subjects had to meet the following criteria: (a) were age 18 or older; and (b) had no abnormal ICP in the medical history. Individuals were excluded if they had any of the following conditions: (a) history of ophthalmological or neurological diseases (orbital tumor [$n = 1$] and stroke [$n = 3$]), (b) intracranial lesions that may affect ICP (intracranial tumor [$n = 5$] and intracranial vascular malformations [$n = 3$]) were found in the written reports of screening MRI, and (c) poor imaging quality due to intense movement or metal artifacts ($n = 3$). In total, 413 individuals were finally included in this study. Each individual recorded the following demographic and

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physiological data: age, sex, weight, height, body mass index (BMI), and the mean arterial blood pressure (MABP, $1/3$ systolic blood pressure + $2/3$ diastolic blood pressure).

MRI in all participants was performed using the GE Discovery MR750 3.0T (General Electric Company, NY, USA). The participants were instructed to keep both eyes closed with minimal movement during the scanning. The axial images were collected parallel to the horizontal plane connecting the anterior and posterior commissures, and the scanning range covered the entire brain. We measured the ONSD and eyeball transverse diameter (ETD) of each eye using TOF-MRA with the imaging parameters as follows: time of repetition = 19 ms, time of echo = 3.4 ms, flip angle = 20° , one signal average, section thickness = 1 mm, field of view = $22.0\text{ cm} \times 22.0\text{ cm}$, and acquisition matrix = 416×224 pixels [Supplementary Figure 1A, <http://links.lww.com/CM9/A450>].

MRI data were independently assessed by two experienced radiologists who were unaware of the sample selection and the participants' clinical data, using an image archive and communication system (iMedPACS V4.1, DHC Software Company, China). The ONSD at 3 mm behind the eye along an axis perpendicular to the optic nerve was measured by enlarging the retrobulbar area by 10 times (zoom factor, 10.0) and then using the electronic calipers to measure.^[1,3] ONSD refers to the distance between the outer edges of the thick sheath that covers the optic nerve. ETD refers to the transverse diameter of the eyeball (retina to retina). Among the axial images, we selected four images showing the maximum ONSD and ETD of each eye for measurement.^[3] To minimize variability, each eye was measured three times, and the average of the 24 measurements was taken as the final value.

All the statistical analysis was performed using the Statistical Product and Service Solutions, version 17.0 (SPSS, Chicago, IL, USA). Continuous variables are presented as mean \pm standard deviation (SD) and median (interquartile range) values, whereas categorical variables are presented as frequencies and percentages. Simple linear regression analyses and multiple regression analysis were conducted to determine the independent factors related to ONSD. All variables for which P was <0.05 in the simple linear regression models were selected in the multiple linear regression model. Two independent sample t tests were used to understand the effect of gender on ONSD and ETD between the gender groups. A two-tailed probability of $P < 0.05$ was used as the significant level.

The ONSD was measured in 413 healthy subjects aged 21 to 88 years (58.0 ± 16.0 years), among whom 227 (55%) were male. The values of ONSD, ETD, and ONSD/ETD ratio, which were measured by MRI, are shown in Supplementary Figure 1B, <http://links.lww.com/CM9/A450>. The ONSD values for both the eyes had no significant difference ($t = -0.116$, $P = 0.908$). We further assessed the relationship between ONSD and age, sex, weight, height, BMI, and MABP. Simple linear regression analysis showed that ONSD was correlated with sex ($P = 0.002$) and ETD ($P = 0.002$). After removing the interference of confounding factors, multiple regression

analysis showed that ONSD was associated with sex ($P < 0.001$) and ETD ($P = 0.001$). Based on the results of multiple linear regression, and in order to study the effect of gender on ONSD, the participants were divided into two groups based on gender. The ONSD and ETD values were significantly different between the two groups ($t = 5.558$, 5.025 ; $P < 0.001$, 0.001). Males had larger ONSD and ETD values than females.

Our research results have shown that the mean values of the ONSD and ONSD/ETD ratio were 4.76 ± 0.43 mm (95% confidence interval [CI], 4.72–4.80 mm) and 0.22 ± 0.02 (95% CI, 0.21–0.22), respectively, which was larger than the ultrasound values (3.57–4.70 mm).^[1] MRI provides images of the eye with a high spatial resolution, allowing for a clear picture of the orbital structure, thus avoiding the disadvantages of ultrasound, such as poor penetration and human interference in the observation.^[3] The above-mentioned disadvantages of ultrasound may be the reason for the inconsistency between the two studies.

Some of the previous studies have determined the normal value of ONSD by MRI as 3 to 5 mm, calculated from behind the eyes of healthy participants.^[3] The mean values of European and American people ranged from 5.08 to 5.72 mm, which are larger than that of Asian people (4.71–5.1 mm).^[3] The reason for such differences may be the racial and/or genetic difference between the European/American and Asian populations.^[1] The results suggest that ethnic differences should be taken into account when interpreting the relationship between ONSD and ICP.

The current results revealed that ONSD was correlated with ETD and sex but not with age, weight, height, BMI, and MABP. Our study has also proposed that sex was significantly associated with ONSD, and that the mean values of ONSD and ETD of the male participants were higher than those of the female participants. Goeres *et al*^[5] assessed 120 healthy adults and demonstrated a different ONSD range between men and women, confirming the impact of gender on ONSD. The reason may be due to the difference in the nerve fiber density between sexes. Using MRI as a measurement tool, this work has the largest population ever studied and a reasonably balanced number of men and women; so, previous studies may not have been able to detect the differences that can be detected here. This suggests that if ONSD as measured by MRI is used as a diagnostic indicator of raised ICP, separate reference ranges may be required for men and women.

In conclusion, the present study found that the mean values of ONSD and ONSD/ETD ratio measured by MRI in healthy Chinese adults were 4.76 mm (95% CI, 4.72–4.80 mm) and 0.22 (95% CI, 0.21–0.22), respectively. The ONSD was significantly associated with ETD and sex. The intersex differences in the ONSD values suggest that separate reference ranges may be required for men and women.

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Conflicts of interest

None.

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