# Computed Tomography Density of the Venous Sinuses in Healthy Patients at 2,600 Meters Above Sea Level

## Densidad escanográfica de los senos venosos en pacientes sanos a 2.600 metros sobre el nivel del mar

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Acronyms:
Hb: Hemoglobin.
Ht: Hematocrit.
ROI: Region of interest
HU: Hounsfield Units

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Imagen por resonancia magnética

## Summary

***Introduction:*** There is a relationship between the intravascular density measured in Hounsfield units (HU) in computed tomography (CT) and the hematocrit levels, which increases in people who live above sea level. The expected density in venous sinuses is lower than 70 HU in healthy people living at 1000 meters above sea level. However, this measure has not been established in people living at higher geographic altitudes. In this study, this value was determined for normal people living at 2,600 meters above sea level. ***Objective:*** The purpose of this study is to characterize the normal density of the venous sinuses in patients who live at geographical altitudes of 2,600 m above sea level. ***Methodology***: We measured the density on CT at the superior longitudinal venous sinus and at the junction between the transverse sinus and sigmoid sinus of 240 subjects living at 2600 meters above sea level from January 2008 to June 2016. These patients consulted for headache, seizures, altered state of consciousness or neurological focus. Initially, all participants had a non-enhanced CT brain, hemoglobin and hematocrit levels with a difference of no more than 3 days between the CT study and the hemogram, as well as confirmatory studies of positivity or absence of intracranial sinus thrombosis by non-enhanced MR or MRA. ***Results:*** The mean HU was 59.8 with a range between 43.2 and 74.9, for normal patients. A positive correlation of 0.49 was found between hematocrit and HU, as is widely known in the literature. Conclusion: We obtained a wide range in the HU of healthy patients compared to the values reported in other papers, and exceeds the highest value by 4 points. This may be attributable to the increased hematocrit in healthy patients living at 2,600 meters above sea level. In order to establish whether patients with venous sinus densities greater than 70 HU have venous thrombosis, our suggestion is to evaluate the symmetry of the density compared to the contralateral venous sinus, as well as to evaluate the morphology and the location of the ROI used to measure venous density.

## Resumen

***Introducción:*** Existe relación entre la densidad escanográfica de las estructuras vasculares medida en unidades Hounsfield (UH) y el hematocrito, el cual se incrementa en las personas que viven a mayor altitud sobre el nivel del mar. Se ha descrito que una densidad de 70 UH es el valor límite superior de normalidad de densidad de los senos venosos en personas sin trombosis venosa que habitan a una altitud de 1.000 m s. n. m.; sin embargo, no se ha establecido esta medida en personas que habitan en altitudes geográficas mayores. En este estudio se determinó dicho valor para personas sin trombosis de senos venosos que viven a 2.600 m s. n. m. ***Objetivo:*** Este estudio tiene como propósito caracterizar la densidad normal de los senos venosos en pacientes que habitan en altitudes geográficas de 2.600 m s. n. m. ***Metodología:*** Se analizaron las densidades escanográficas de los senos venosos longitudinal superior y de los sitios de unión entre los senos transversos y senos sigmoides de 240 sujetos que habitan a 2.600 m s. n. m., quienes asistieron a la institución entre enero de 2008 y junio de 2016.

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Estas personas consultaron por cefalea, convulsiones, alteración del estado de conciencia o focalización neurológica. A estos pacientes se les realizó inicialmente un estudio escanográfico de cráneo simple, hemoglobina y hematocrito con diferencia no mayor a 3 días entre el estudio escanográfico y el hemograma, así como estudios confirmatorios de positividad o ausencia de trombosis de senos intracraneales mediante resonancia magnética simple o angiorresonancia. ***Resultados:*** La media de UH fue de 59,8 con un rango entre 43,2 y 74,9, para pacientes normales. Se encontró una correlación positiva de 0,49 entre el hematocrito y las UH como es ampliamente conocido en la literatura. ***Conclusión:*** El rango en UH de los pacientes sin trombosis de senos venosos es amplio y supera por 4 puntos el informado en la literatura. Esto puede ser atribuible al aumento del hematocrito en individuos que viven a 2.600 m s. n. m. Para establecer normalidad en los pacientes con valores superiores a 70 UH se sugiere tomar en cuenta la simetría de la densidad escanográfica con respecto al seno venoso contralateral, así como evaluar la morfología del borde anterior del seno venoso y la adecuada localización del ROI *(Region of Interest)* para medir la densidad venosa.

## 1. Introduction

Nowadays, diagnostic image visualization programs in digital format allow the measurement of the density of the different body structures in the scanning modality, also called computed tomography (CT). This density is expressed globally in Hounsfield units (HU) and is obtained automatically by the image viewing program. The measurement is obtained by selecting an area of interest (ROI) that should cover approximately 75% of the area of the structure to be measured.

Despite the widely accepted relationship between scan density and hematocrit, no normal cut-off values of intracranial venous sinus density have been defined in normal persons to differentiate them from patients with venous sinus thrombosis at geographic altitudes greater than 1,000 m. a.s.l.. The suspicion of venous sinus thrombosis is based on subjective assessments when visualizing a higher than usual density in these vascular structures while evaluating an imaging study. In the institution where the present study was performed, located at a geographical altitude of 2,600 m. a.s.l., frequent interobserver variability has been observed, as well as underdiagnosis of this pathology. High density of intracranial vascular structures is commonly attributed to high hematocrit values.

In order for the evaluation of imaging studies in patients with suspected venous sinus thrombosis to be objective, quantitative measurement of venous sinus density in HU should be performed. There is a positive correlation (r = 0.840) between vascular density measured in HU and hematocrit value (1). It is known that the higher the geographic altitude, the higher the intravascular erythrocyte concentration (hematocrit); therefore, vascular density values are higher at higher geographic altitudes.

At higher altitudes above sea level, the ambient oxygen concentration is lower; as a compensatory body mechanism, people who live or ascend to geographical altitudes higher than 2,500 meters above sea level increase their erythrocyte concentration due to a higher production of erythropoietin (2), which increases hematocrit levels. Consequently, higher vascular density can be observed (3, 4).

Hematocrit is defined as the percentage of erythrocyte mass in 100 mL of blood. The normal ranges in adult women and men in Bogota, located approximately 2,600 m. a. s. n. m., are between 43-50 % and 45-53 %, respectively (5). In the last 15 years, in studies carried out with the purpose of identifying states of anemia by means of images, a correlation between hemoglobin levels and vascular density in different body structures has been demonstrated (6, 7). Vascular density should be quantified in simple scanography, because intravenous iodinated contrast media significantly increase the values of this density.

It has been reported that 70 HU is the maximum normal value of density in vascular structures in people living at sea level. Higher values raise suspicion of intracranial venous sinus thrombosis (8). None of the patients without venous sinus thrombosis in that study showed density values higher than 70 HU. For the care of people living at higher altitudes above sea level, it is considered important to conduct a study to establish vascular density values in patients without venous sinus thrombosis.

Performing an objective measurement of venous sinus density and characterizing this population by the increase in hematocrit - and, therefore, in density - will allow alerting about the appearance of entities, such as venous sinus thrombosis, with lesser long-term neurological consequences.

## 2. Methods

After the approval of the ethics committee of the institutions involved, a review of the medical records and scan images, simple magnetic resonance and angioresonance of 243 patients, between 2008 and 2016, without venous sinus thrombosis confirmed by cerebral magnetic resonance as in figures 1 and 2 was performed. In the process of analysis, three patients without venous sinus thrombosis were identified and excluded from the study, in whom insufficient clinical data were found, and one who did not meet the technical factors for the measurement.

Venous sinus measurements were also performed in patients with a diagnosis of venous sinus thrombosis who had a confirmatory MRI study (Figures 3, 4 and 5).

### *2.1. Population*

The patients were over 18 years of age with normal simple brain scan, who also underwent MRI and complete blood count, with a time difference between the laboratory studies of no more than 3 days with respect to the scan.

Patients with any intracranial device or lesions that produced artifact or alteration of venous sinus density were excluded. Also, patients with intracranial hemorrhage, history of recent trauma and intracranial pathology other than venous sinus thrombosis that produced morphological alteration in the scan. Finally, patients who had been administered intravenous contrast medium during the 3 days prior to the single brain scan study were not included.

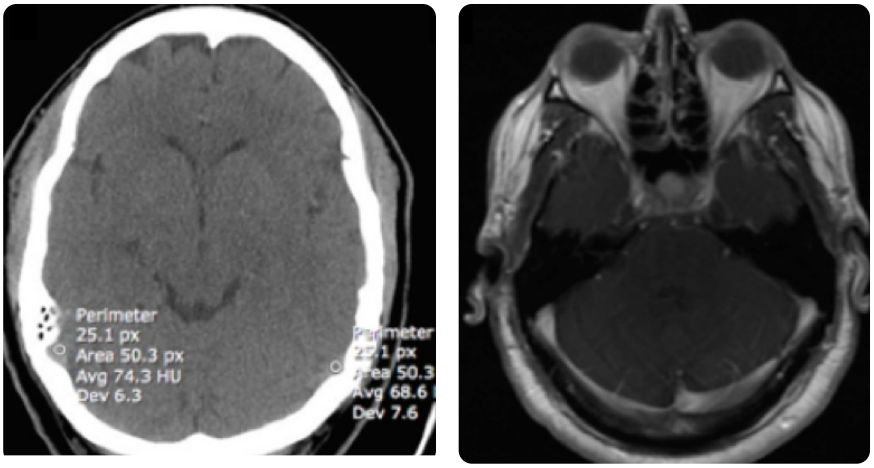


Figure 1. 49-year-old man with headache, Hb: 19.1 g/dL, Ht: 59. a) Axial scan section without contrast medium. Increased venous density with values higher than 65 HU in the left transverse sinus and 70 HU in the right. b) Axial MR image spin echo sequence with T1 information with contrast medium. There is evidence of transverse sinus patency, which confirms that there is no thrombosis.

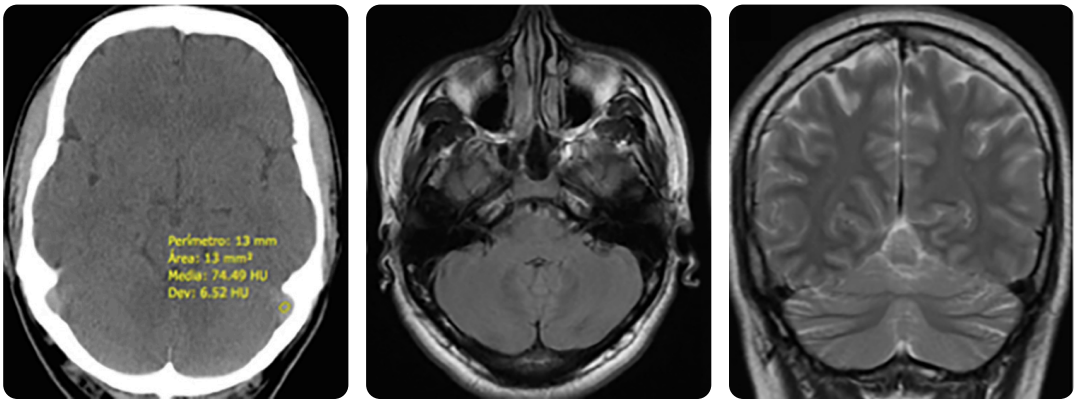


Figure 2. 32-year-old man with headache, Hb: 17.3 g/dL, Ht: 50.3. a) Axial scan section without contrast medium. Increased venous density in left transverse sinus with density of 74 HU in this location. b and c) Axial and coronal MR image, spin-echo sequences with T1 and T2 information, respectively, without alteration in the empty flow sign or in the morphology of the venous sinus contours.

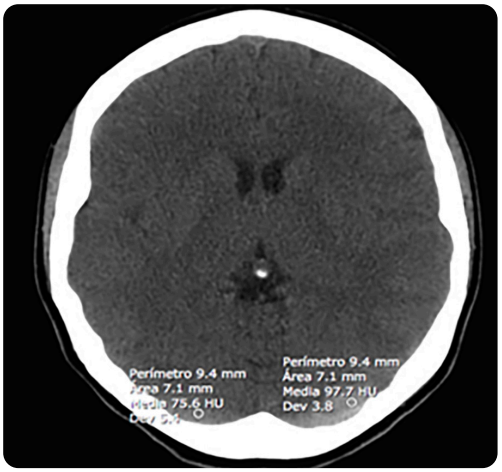


Figure 3. 21-year-old woman with headache and vertigo. Axial scan section without contrast medium. There is asymmetry in the density of the transverse sinuses and significant increase in the density of the left transverse sinus with indicative value of thrombosis.

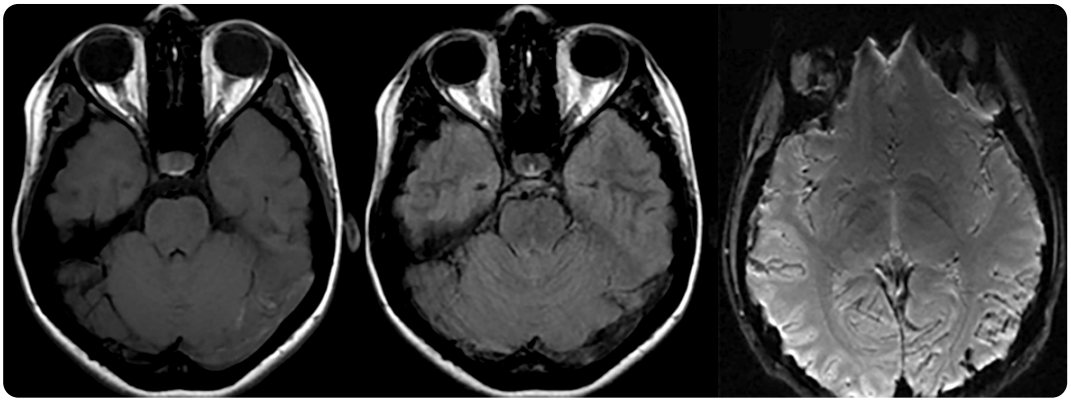

Figure 4. Same patient of previous imaging study. Brain MRI study. a) Axial image, spin echo sequence with T1 information: prominence and increase in signal intensity of the left transverse sinus due to thrombosis. b) Axial T2 FLAIR: alteration of the flow void sign of the left transverse sinus, convex configuration of the anterior contour. c) Axial Magnetic Susceptibility. Low signal of left transverse sinus, superior longitudinal sinus and some occipital cortical veins due to thrombosis.

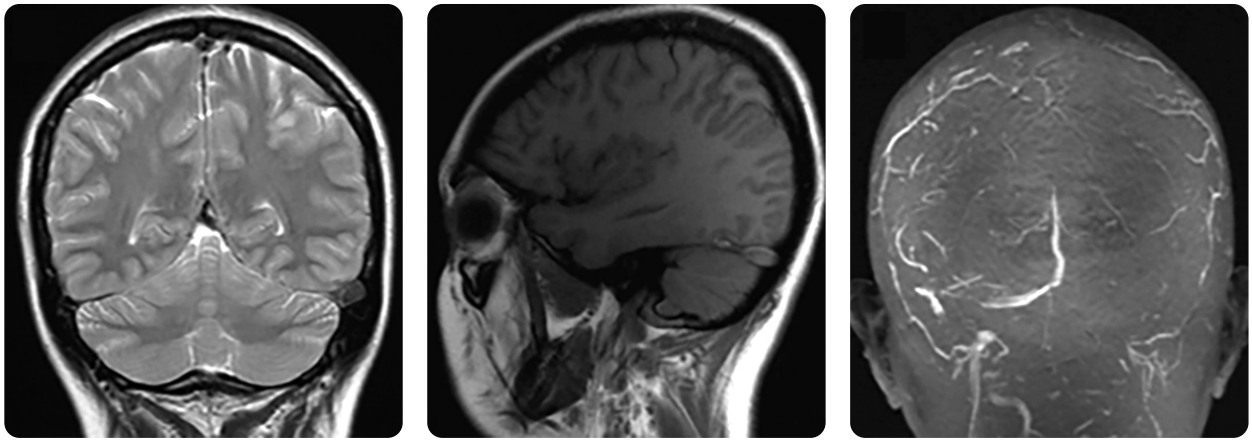

Figure 5. Same patient of previous imaging study. Brain study and MR venography. a) Coronal spin-echo sequence with T2 information. Prominence and heterogeneity in the signal intensity of the superior longitudinal and left transverse sinuses due to thrombosis, convex contours of the different borders of the vascular structure. b) Sagittal T1 Flair. Increase in the signal intensity of the left transverse sinus and anterior and superior convex contour. c) MR venography. Absence of vascular flow in an extensive segment of the superior longitudinal sinus, as well as in the totality of the left transverse and sigmoid venous sinus.

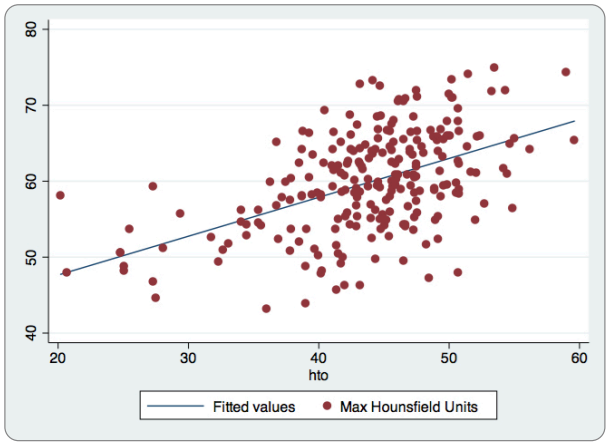


Figure 6. Relationship between scan density (HU) and hematocrit of the studied population without venous sinus thrombosis, showing a positive correlation of 0.49. In addition, scan density values higher than 70 HU are observed, with a maximum value of 74.9 HU.

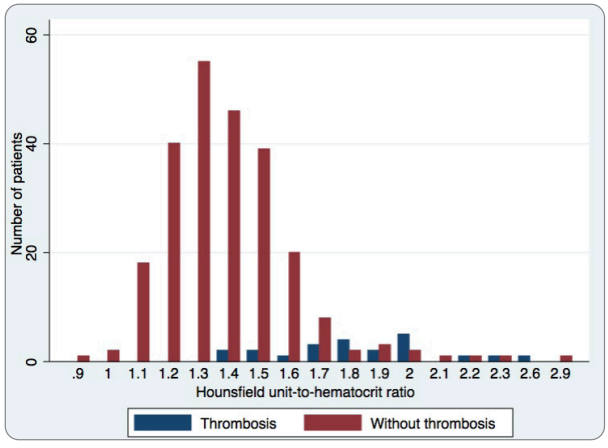


Figure 7. Number of patients with H:H ratio values both in the group of patients with venous sinus thrombosis (blue) and in the group without venous sinus thrombosis (red). The cut-off value above which thrombosis occurred was 1.4.

### *2.2. Sample size*

In order to establish an upper limit of normality for people living at 2,600 m. a. s. n. m., density measurements were performed in 240 patients from 2008 to 2016 in single brain CT studies, who met the inclusion criteria. This sample size exceeds the largest sample reported in the literature, which is 166 patients (1). Note that consecutive sampling was performed in this study given that all available patients with a diagnosis of venous sinus thrombosis with CT and MRI, and hematocrit were selected.

## 3. Materials

The scans included in the study were performed on a General Electric Light Vision VCT tomograph and the images were acquired using the following technical parameters: 120 kilovolts, 300 milliamps, slice thickness of 5 mm, rotation time of 1.20 detectors and FOV (field of view) of 240 mm.

Measurement of venous sinus density in patients without thrombosis was performed at three sites: the confluence of the sinuses, the lower third of the superior longitudinal sinus, and at the right and left transverse-sigmoid junctions. For this measurement an ROI was used with areas between 6 and 15 mm² occupying between 40 and 75 % of the caliber of the sinus to be measured, as shown in Figure 3.

### *3.1 Statistical analysis*

Statistical measures of central tendency were used to describe and plot the data. The Shapiro-Wilk test was used to determine whether the sample follows a normal distribution. Likewise, a correlation test was performed between hematocrit and vascular density measured in HU. Statistical analysis was performed using STATA 12.

## 4. Results

A total of 240 patients without venous sinus thrombosis were studied, with a mean age of 47 years (range 18 to 97 years), the majority were men, 122 subjects (51 %). The mean hemoglobin in this

population was 14.59 (range 6.6-19.1), hematocrit had a mean of 43.86 with a range of 20.2 to 59.6 (Tables 1 and 2). In addition, the scan density in venous sinuses of 22 patients with confirmed thrombosis was evaluated (Table 3).

The results of the ranges, mean and median venous density in HU, hemoglobin, hematocrit, and HU:Ht ratio are shown below.

**Table 1. Characteristics of individuals without venous sinus thrombosis randomly taken as control group**

| Characteristics | Mean | Median | Min | Max |
|---|---|---|---|---|
| Age | 46.63768 | | 18 | 82 |
| HU | 60.34464 | 59.85 | 46.3 | 74.6 |
| Hemoglobin | 14.72754 | 14.9 | 7.1 | 18.7 |
| Hematocrit | 44.41159 | 44.7 | 20.7 | 56.2 |
| H:H | 1.381159 | 1.4 | 1.1 | 2.3 |

**Note:** H:H= HU/Ht ratio.

**Table 2. Characteristics of women and men without venous sinus thrombosis**

| Women | | | | |
|---|---|---|---|---|
| Characteristics | Mean | Median | Min | Max |
| Age | 45.82 | 42.5 | 18 | 92 |
| HU | 58.47 | 59.05 | 43.8 | 71.8 |
| Hemoglobin | 13.67 | 14.1 | 6.6 | 18.1 |
| Hematocrit | 41.19 | 42.2 | 20.2 | 53.3 |
| H:H | 1.44 | 1.4 | 1.1 | 2.9 |
| **Males** | | | | |
| Age | 48.72 | 49.5 | 18 | 97 |
| HU | 61.19 | 61.25 | 43.2 | 74.9 |
| Hemoglobin | 15.48 | 15.8 | 7.9 | 19.1 |
| Hematocrit | 46.44 | 47.3 | 24.8 | 59.6 |
| H:H | 1.33 | 1.3 | 0.9 | 2 |

**Table 3. Characteristics of the total number of patients with venous sinus thrombosis**

| Characteristics | Media | Mediana | Min | Max |
|---|---|---|---|---|
| Age | 40.86 | | 19 | 94 |
| HU | 75.5 | 76.9 | 69.2 | 97.6 |
| Hemoglobin | 14.5 | 43.9 | 10.1 | 17.2 |
| Hematocrit | 43.7 | 14.4 | 31.1 | 53.5 |
| H:H | 1.8 | 1.7 | 1.4 | 2.6 |

Table 4 shows the maximum and minimum density values as well as the mean transverse venous sinus and sinus confluence values separately in men and women without venous sinus thrombosis.

**Table 4. Density of venous sinuses measured in Hounsfield units in patients without venous thrombosis according to location**

| Women | | | | |
|---|---|---|---|---|
| Characteristics | Mean | Median | Min | Max |
| Right transverse sinus | 57.11 | 56.5 | 38 | 71.8 |
| Left transverse sinus | 56.17 | 57.8 | 40.7 | 74.1 |
| Confluence of breasts | 51.08 | 43.9 | 32.8 | 67.5 |
| **Males** | | | | |
| Right transverse sinus | 58.89 | 60 | 31.2 | 74.9 |
| Left transverse sinus | 59.36 | 59.4 | 31.4 | 74.1 |
| Confluence of breasts | 52.95 | 53.05 | 36.6 | 71.3 |

A positive correlation of 0.49 was established between Ht and HU in patients without venous sinus thrombosis, as shown in Figure 6. The mean HU-Ht ratio was 1.4 (range 0.9-2.9).

The mean maximum HU was 59.8 with a range of 43.2 to 74.9 (Shapiro-Wilk p 0.61549, failure to reject the null hypothesis of normality). Additionally, a positive correlation between hematocrit and HU of 0.5 is obtained, as shown in Figure 6.

The cut-off value of 1.8 in the H:H ratio (HU:Ht) suggested by Black et al. (8) and 1.5 suggested by Buick et al. (9), did not coincide with the findings in our population, which did present overlapping in the distribution of the values of the ratio (Figure 7), documenting H:H ratio values of up to 1.4 in patients with thrombosis (Table 5), since when presenting higher levels of hematocrit the value of the H:H ratio decreases.

**Table 5. H:H ratio**

| Males | | | | |
|---|---|---|---|---|
| Characteristics | Mean | Median | Min | Max |
| H:H | 1,33 | 1,3 | 0,9 | 2 |
| **Women** | | | | |
| H:H | 1,44 | 1,4 | 1 | 2,9 |

## 5. Discussion

The positive correlation between hematocrit and vascular density measured in HU has been widely documented in the literature. Likewise, a directly proportional relationship has been established between geographic altitude and increased hematocrit (1-3, 8, 9). Therefore, it is expected that the higher the altitude, the higher the values of vascular density measured in HU.

Comparatively, while in the study by Black et al. (8) none of the controls had values higher than 70 HU, in the present work 18 patients without venous sinus thrombosis were found to have vascular density higher than 70 HU, in a normally distributed healthy population; a maximum value of 74.9 HU was obtained.

Note that the density in the aforementioned study was measured at the confluence of the venous sinuses, as in our study. With the exception that in our investigation the transverse-sigmoid junction was also measured. These populations are not comparable because the height

in Bogota is greater than that of the city where the study by Black et al. was performed.

It should be mentioned that 9 of the 18 healthy controls with density greater than 70 HU had hemoglobin and hematocrit values higher than expected -only because they lived at high altitude- and were considered cases of polyglobulia (hemoglobin levels > 16 g/dL in women and > 16.5 g/dL in men or hematocrit and hematocrit > 48% in women and > 49% in men) (10); Therefore, polyglobulia should be considered as a differential diagnosis in the finding of high density of venous sinuses, especially at altitudes equal or higher than 2. 600 m. a. s. n. m., where, as a physiological response to the lower amount of oxygen, hemoglobin and hematocrit levels are higher. On the other hand, of the total population, 43 had polyglobulia criteria and no venous sinus density values higher than 70 HU were found.

In this study, the time between the onset of symptoms and the imaging study was not taken into account; therefore, it was not possible to define the relationship between density and chronicity of the thrombotic event. The time of evolution of the thrombotic event alters the density of the thrombus, its density being higher during the acute phase of thrombosis and decreasing progressively in subacute and chronic phases. Partial recanalization of the vessel would also decrease its density, therefore low values of scan density do not rule out non-acute thrombotic events or with recanalization. The presentation of the thrombus in MRI is variable due to changes in the state of hemoglobin degradation; in spin echo sequences it may show absence of the signal void sign, with medium intensity in T1 and low signal in T2 in the acute phase, while in the subacute phase high signal in T1 is observed. The gradient echo sequence with T1 information with contrast medium provides the highest sensitivity and specificity for thrombus detection.

Other research groups, such as Alsafi et al. (11), have compared the relation between the density of thrombosed venous sinuses with the average density of the intracranial internal carotid arteries and have referred a relation greater than 1.5 as highly suggestive of venous sinus thrombosis; however, the purpose of our study was focused exclusively on the analysis of the density of venous sinuses, since the relations with other vascular structures implies more time in the diagnostic approach. The frequent compromise of calcified atheromatous compromise may alter the arterial density values and, consequently, the relationship of the thrombosed sinus density with the average arterial density in supraclinoid internal carotid arteries and the basilar artery.

## 6. Conclusion

Again, a positive correlation between imaging density and hematocrit was demonstrated, with values up to 74.9 HU in patients without venous sinus thrombosis, which is 5 HU higher than that documented in previous studies in populations living at lower geographic altitudes. The minimum density value in patients with venous sinus thrombosis was 69.2 HU; however, the time of the thrombotic event was not defined in this study.

Based on the results obtained in the present study, it is considered appropriate that in patients with values between 69 and 74.9 HU who live at similar geographic altitudes to Bogotá, other scanographic characteristics suggestive of venous sinus thrombosis should be evaluated, such as the convex configuration in the anterior and superior contours of the transverse sinuses, especially in the sagittal plane; it is also considered useful to evaluate asymmetry in the density and caliber of the venous sinuses, as long as hypoplasia of the contralateral venous sinus and other anatomical variants are excluded (12).

It must be considered that there are several technical factors that may alter the density measurement, among these, artifacts due to beam hardening secondary to the presence of intra or extracranial devices, as well as variations from one scanner to another (13).

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