Echocardiographic evaluation of inferior vena cava diameters and collapsibility index in healthy children

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ABSTRACT

Introduction. Echocardiographic measurement of inferior vena cava diameters and collapsibility index (IVCCI) can estimate right heart chamber function and intravascular volume status. Few reports of reference values for diameters and IVCCI in the pediatric population exist. This exploratory study aimed to understand the behavior of diameters and IVCCI as a function of body surface area (BSA) in healthy children to establish possible reference values in the future.

Population and methods. Ninety-nine Mexican children aged 12 to 204 months were included. Anthropometry and transthoracic M-mode echocardiography were performed to assess the maximum expiratory diameter (MAXDE) and the minimum inspiratory diameter (MINDI). IVCCI was calculated with the formula (MAXDE - MINDI) / MAXDE × 100.

Results. A linear regression model was performed to calculate the predicted values (mean ± 2 standard deviations of MAXDE and MINDI expressed per BSA). The predicted value of the IVCCI for each representative BSA value was calculated from the MAXDE and MINDI values predicted by the model.

Conclusions. Variations were found in the values of diameters and IVCCI concerning studies performed in other pediatric groups. This indicates the importance of having specific reference values for each population and opens the door to generating more research in healthy children and even those with cardiac disorders.

Keywords: *echocardiography; inferior vena cava; respiration; reference values; child.*

doi: http://dx.doi.org/10.5546/aap.2024-10384.eng

To cite: Corres-Molina M, Rodríguez-Cuevas JL, Cardoso-Enciso HR, Mejía-Terrazas GE, López-Muñoz E. Echocardiographic evaluation of inferior vena cava diameters and collapsibility index in healthy children. *Arch Argent Pediatr.* 2025;e202410384. Online ahead of print 23-JAN-2025.

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Financing*: None.*

Conflict of interest*: None.*

Received*: 3-25-2024*
Accepted*: 11-19-2024*

INTRODUCTION

Transthoracic echocardiography is a noninvasive method that provides information on the anatomy, hemodynamics, and physiology of the heart, heart valves, and great vessels.[1-3]

It plays a key role in detecting pressure changes or vascular flows and is therefore considered an excellent method for evaluating cardiac cavities and right vascular structures, including the inferior vena cava (IVC).[4,5]

The IVC is a vascular structure whose diameter and dynamics are sensitive to pressure and volume changes. Its collapse depends on the pressure within its lumen, increased intra-abdominal pressure, or a combination of both. During inspiration in spontaneous ventilation, there is an increase in negative intrathoracic pressure, increased blood flow to the right atrium, and decreased pressure in the IVC with transient collapse and reduction of its diameter; during expiration, the opposite occurs.[6] Evaluation of its diameter and ventilatory response reflects the hemodynamics of the right heart chambers and central blood volume, allowing indirect estimation of central venous pressure (CVP) or right atrial pressure (RAP).[6-10]

The most used ventilatory response indices of the IVC are the inspiratory collapse index or IVC collapsibility index [IVCCI = maximal expiratory diameter (MAXDE) - minimal inspiratory diameter (MINDI)/MAXDE × 100] in spontaneously ventilated patients[6-8,11] and the IVC distensibility index [IVCDI = maximal inspiratory diameter (MAXDI) - minimal expiratory diameter (MINDE)/MAXDI × 100] in mechanically ventilated patients.[12-15]

IVCCI and IVCDI, both static and during contractility,[16] can be used in place of CVP and RAP to estimate right cardiac chamber function and intravascular volume status,[17], and to guide fluid therapy.[10,12,18,19]

The usefulness of assessing IVCCI in children has not been fully demonstrated. Some studies have reported a significant correlation of IVCCI with CVP in children with hemodynamic monitoring in intensive care units (including newborns),[18,20] with cardiovascular disease,[21] in shock,[22] and the perioperative period of cardiac surgery.[23] It has also been shown to reduce IVC diameter in children with dehydration[24] and increase it with intravenous fluid replacement.[22,24] However, the reference values reported in children are scarce and heterogeneous, considerably limiting their clinical use.

Given the potential that echocardiographic measurements of the IVC could have for assessing intravascular volume status and, indirectly, RAP and CVP, this exploratory study aimed to determine the behavior of diameters and IVCCI as a function of body surface area (BSA) in healthy children, so that possible reference values could be established in the future.

POPULATION AND METHODS

Patient selection

Observational, descriptive, and prospective exploratory study approved by the Research Ethics Committee of the Naval Medical Center of the Secretariat of the Navy, Mexico City, Mexico (Registration number 016/2019). The procedures were performed by the Declaration of Helsinki and national and international ethical standards for research on human subjects. The participants' parents gave written informed consent, and the under-aged assented when applicable.

Healthy children between 12 and 204 months (17 years) who attended growth and development control at the Pediatric Clinic of the Naval Medical Center, Mexico City, between January 1, 2019, and December 31, 2020. All participants underwent clinical history, anthropometry, and transthoracic echocardiography.

Sex, age, weight, height, and BSA were recorded according to the Haycock formula.[25,26] In those older than 2 years, body mass index (BMI) was calculated by dividing kilograms of weight by the square of height in meters.[27] Anthropometric values were within the 3rd to 97th percentiles for their age according to the growth charts of the Centers for Disease Control and Prevention (CDC)[27] and the World Health Organization (WHO).[28]

Individuals whose anthropometry was found to be outside the normal percentiles for their age, with clinical signs of dehydration and a history of pulmonary and/or cardiac disease (congenital or acquired), who were detected with cardiac anomalies or who did not conclude the echocardiographic evaluation due to uncontrollable crying.

Echocardiographic evaluation

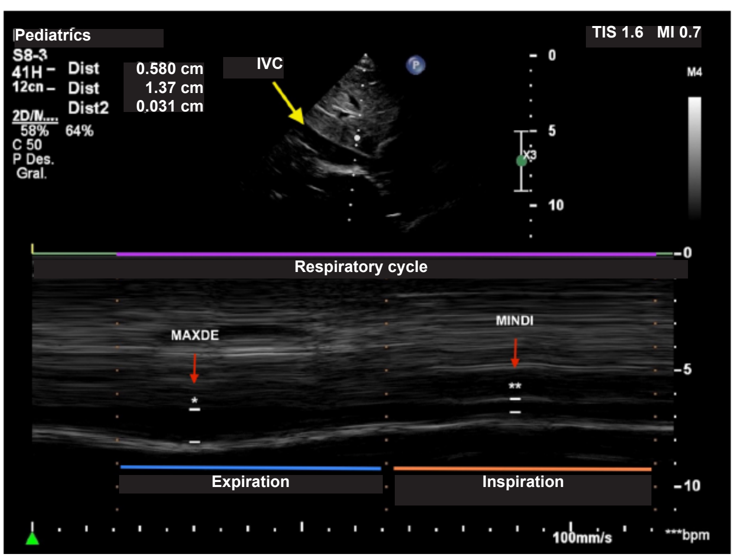
A pediatric cardiologist performed it. Phillips EPIQ 5® ultrasound with S12-4 transducer (12-4 MHz; 9.78 mm aperture) was used for children under 2 years, and S8-3 transducer (8-3 MHz; 1.4 mm opening) for those older than 2 years. Echocardiography was performed in the presence and with parental assistance, with the patient in left lateral supine decubitus, conventional transthoracic, and subcostal echocardiographic windows and identifying variations in the respiratory cycle without stress or crying.

The type and mode of atrioventricular and ventriculo-arterial connections were identified, corroborating the absence of cardiac malformations. The integrity of the interatrial and interventricular septa was verified, ruling out shunts. To confirm adequate cardiac function, the tricuspid regurgitation gradient determined the left ventricular ejection fraction, fractional shortening, and right ventricular systolic pressure. For IVC assessment, the abdominal situs was identified with a subcostal axial plane in two-dimensional mode, and the transducer was rotated at 90° to obtain the major axis of the junction of the IVC with the right atrium. Once the anterior and posterior wall of the IVC above the junction of the suprahepatic veins was identified, the M-mode was applied, obtaining measurements in inspiration and expiration during the same respiratory cycle (*Figure 1*).[25,29] IVCCI was calculated with the formula previously described.[6-8,11]

Statistical analysis

Consecutive case sampling was performed, with sample size per study period. Qualitative variables are presented as relative frequencies. Quantitative variables are presented as mean and standard deviation (SD) when their distribution was close to normal (Kolmogorov-Smirnov test) and as median, minimum, and maximum when it was not close to normal. Spearman correlation of age, weight, height, BMI, and BSA with MAXDE, MINDI, and IVCCI was performed. Linear regression analysis examined the relationship between clinical and echocardiographic variables. The model with the highest R^2, statistically significant linear dependence (F statistic), normality of the standardized residuals (Shapiro-Wilk [SW] statistic), independence (Durbin-Watson [DW] statistic), and homoscedasticity (scatterplot analysis between standardized residuals and the standardized values predicted by the model, as well as the Breusch-Pagan [BP]). Graphical analysis of standardized residuals (95% of values between -1.96 and +1.96) was performed. Outliers to be excluded from the analysis were identified visually and confirmed by case-by-case diagnostics. Extreme observations were removed from the final analysis. Model-predicted values (mean ± 2 SD) of MAXDE and MINDI and the expected value of IVCCI were calculated using the formula IVCCI = (MAXDE - MINDI/MAXDE) × 100. The z-score was calculated by dividing the residual values by the standard error of the residual value in the model. The statistical software IBM SPSS version 25® and XLSTAT 2021.3.1® for Mac were used,

Figure 1. Ultrasound image of the inferior vena cava (IVC)



In M mode, the maximum expiratory diameter (mm) (MAXDE) and the minimum inspiratory diameter (mm) (MINDI)** are displayed.*

and p-values <0.05 were considered statistically significant.

RESULTS

A total of 150 children under 204 months were identified; in 16 cases, the parents did not authorize their participation; in 10 cases, the anthropometric measurements were outside the normal range; in 25 cases, the echocardiographic evaluation was not concluded due to uncontrollable crying. Therefore, anthropometric and echocardiographic measurements were obtained from 99 children between 17 and 199 months (58/99 women) (*Table 1*).

A statistically significant correlation of BSA with MAXDE (*rho* = 0.808; p = 0.001), MINDI (*rho* = 0.762; p = 0.001) and IVCCI (*rho* = -0.500; p = 0.001) was observed; of age with MAXDE (*rho* = 0.804; p = 0.001), MINDI (*rho* = 0.752; p = 0.001) and IVCCI (*rho* = -0.481; p = 0.001); and BMI with MAXDE (*rho* = 0.578; p = 0.001), MINDI (*rho* = 0.558; p = 0.001) and IVCCI (*rho* = -0.366; p = 0.001).

MAXDE, MINDI, and IVCCI were modeled using BSA, age, and BMI. Linear, logarithmic, exponential, quadratic, and cubic models were evaluated to identify the best fit. According to R^2 values, the best model with statistically significant linear dependence, normality of standardized residuals, independence, and homoscedasticity was BSA as the independent variable to predict MAXDE and MINDI values. No significant confounding effects of sex were found (MAXDE, p = 0.64 and MINDI, p = 0.081).

The regression equations of the best model to predict the MAXDE (R^2 = 0.661; F= 183.11; p = 0.001. SW = 0.978; p = 0.101. DW = 2.153 and BP = 3.019; p = 0.08) and MINDI (R^2 = 0.566; F= 122.56; p = 0.001. SW = 0.986; p = 0.397. DW = 2.213 and BP = 0.85; p = 0.354) using BSA as the independent variable were:

1) MAXDE = 3.52218303062938 + 7.74442361564213 x BSA
2) MINDI = 0.675523715648521 + 4.97313288551856 x BSA

Once the models with the best fit were identified, the predicted values of the mean and ± 2 SD (*Figures 2* and *3*) of the MAXDE and MINDI as a function of BSA were calculated; subsequently, the expected value of the IVCCI was calculated with the formula described above (*Figure 4*).

DISCUSSION

In adults, assessment of diameters and IVCCI has been proposed as a noninvasive method to estimate CVP or RAP.[30] However, the recommendations for pediatric echocardiographic evaluations do not include reference values for diameters or IVCCI,[29] so it is very important to have these values.

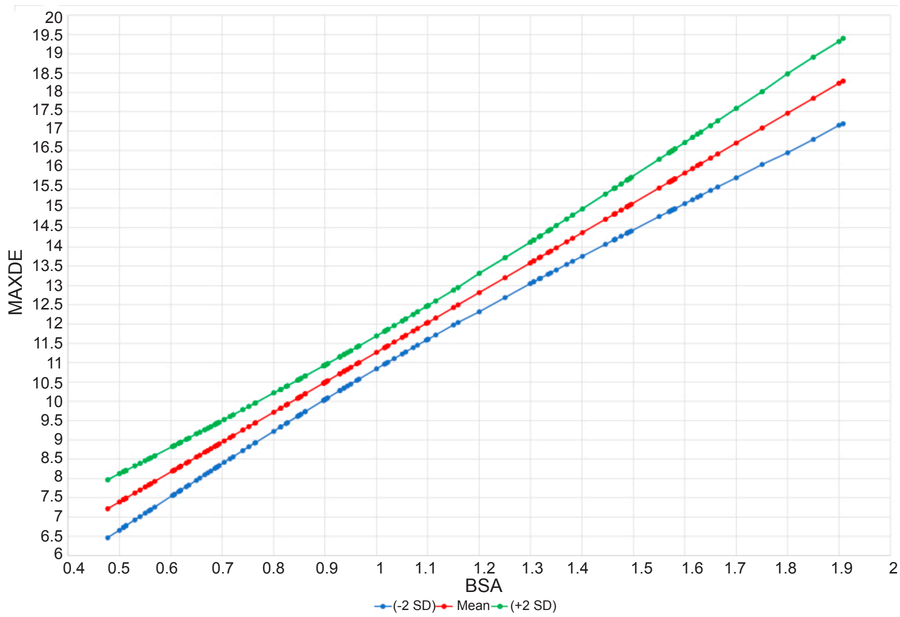
In children, BSA is greater than the results are based on age, weight, and height to estimate the standard measurements of cardiovascular structures. A direct correlation between IVC diameters with age and BSA has been reported in children residing in the United States,[17,31-35] and with other anthropometric parameters such as

Table 1. Quantitative variables evaluated

	Mean*/median**	SD/min.-max.
Age (months)	100**	17-199
Weight (kg)	24.4**	9.6-75
Size (m)	1.25**	0.79-1.73
BMI (kg/m^2)	16.26**	9.23-25.44
BSA (m^2)	0.93**	0.48-1.91
LVEF (%)	69.5*	± 5.1
SF (%)	38.3**	21.1-49.2
TRG (mm of Hg)	19**	10-31
MAXDE (mm)	11.5*	± 3.83
MINDI (mm)	5.9*	± 2.77
IVCCI (%)	50.6*	± 11.99

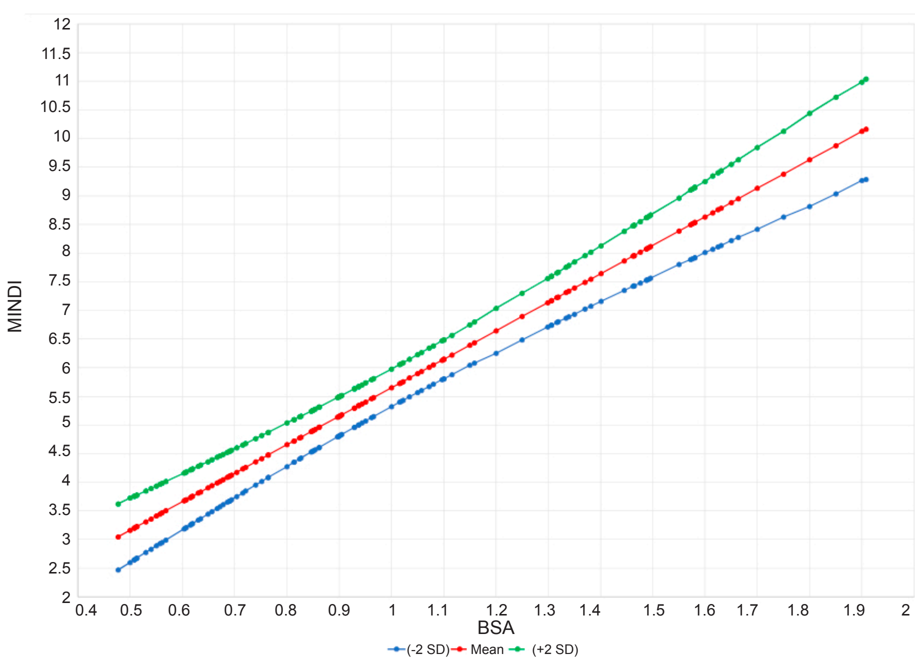
SF, shortening fraction; BMI, body mass index; BSA, body surface area; LVEF, left ventricular ejection fraction; TRG, tricuspid regurgitation gradient; MAXDE, maximum expiratory diameter; MINDI, minimum inspiratory diameter; IVCCI, inferior vena cava collapsibility index; Max., maximum; Min., minimum; SD, standard deviation.

Figure 2. Maximum expiratory diameter (mm) (MAXDE) of the inferior vena cava (IVC) in Mexican pediatric population



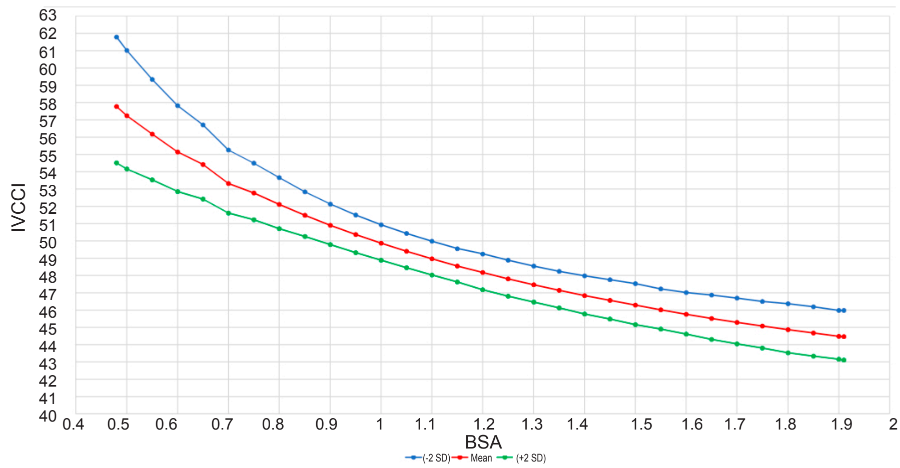
Predicted values of the mean ± 2 standard deviations (SD) according to body surface area (BSA) expressed in square meters (m^2*).*

Figure 3. Minimum inspiratory diameter (mm) (MINDI) of the inferior vena cava (IVC) in Mexican pediatric population



Predicted values of the mean ± 2 standard deviations (SD) according to body surface area (BSA) expressed in square meters (m^2*).*

Figure 4. Collapsibility index (%) of the inferior vena cava (IVC) in Mexican pediatric population



Predicted values of the mean ± 2 standard deviations (SD) according to body surface area (BSA) expressed in square meters (m²).

weight,[33] height,[17,33] and, less frequently, BMI.[17] In our population, although we observed statistically significant correlations between MAXDE, MINDI, and IVCCI with weight, height, and BMI, the best correlations were observed with BSA, similar to that reported by Cantinotti et al.,[26] who used this formula to perform echocardiographic nomograms of cardiac structures in children. For this reason, we used the BSA to calculate the predicted values of the IVC using a linear regression model and thus to elaborate tables and graphs with the values obtained. The graphs of predicted values for MAXDE, MINDI, and IVCCI as a function of BSA allow for a quick visual approximation of the values.

Our study highlights the importance of the population differences observed in the IVCCI measurements. The values observed for mean MAXDE (11.5 ± 3.8 mm), MINDI (5.9 ± 2.77 mm), and IVCCI (50.6 ± 11.99%) in our population showed differences from those reported in 120 healthy US children aged 1-18 years, where mean MAXDE was 12.1 ± 3.8 mm, MINDI 8.9 ± 3.8 mm, and IVCCI 30 ± 13.2%. However, the ranges of MAXDE (3.51-22 *vs.* 4.4-24.4), MINDI (1.0-15.3 *vs.* 1.9-19.2) and IVCCI (13.07-83.87 *vs.* 17.0-64.2) had considerable variation in both our population and the US population.[35]

In another study in 516 healthy Italian Caucasian children aged 1 month to 16 years, the mean MAXDE was 11.6 ± 4.9 mm, MINDI 8.2 ± 4.4 mm, and IVCCI 36 ± 16% in <4 years and 30 ± 17% in ≥4 years; also, with considerable variations in the range of both diameters.[33] The main difference concerning our population is found in the mean MINDI and, consequently, in the mean IVCCI, which the small sample size and the heterogeneity in the age of the children in our study can explain. In addition, we observed lower MINDI values and, therefore, higher IVCCI values in children under 5 years of age, an age in which respiratory frequency, rhythm, and effort can increase inspiratory pressure more easily.[35]

Because of the large variability reported in different pediatric populations in the ranges of MAXDE, MINDI, and IVCCI related to the age, including ours, knowing each measurement's upper and lower limits is more helpful than the absolute mean value.[35]

Regarding measurements as a function of sex, similar to what was observed in healthy Italian Caucasian children,[33] we did not observe differences between males and females in the linear regression models of MAXDE and MINDI, so the predicted values can be used in both sexes.

For now, the predicted values of diameters and IVCCI in this exploratory study should be used with caution. Further studies with a larger sample size are needed to evaluate each measurement's mean, SD, and range for each age group. Weaknesses of our study include a small sample size with significant variability in age and, thus, in BSA. Assessment of hydration status was performed by clinical examination without considering variations in water intake before echocardiography. The echocardiographic evaluations were performed by a single evaluator with the same ultrasound equipment, which reduces the variability that can be attributed to different observers and equipment but makes it impossible to determine the reproducibility and repeatability of the measurements.

CONCLUSION

Our study is the first to estimate the behavior and propose possible reference values for echocardiographic measurement of diameters and IVCCI in a healthy Mexican pediatric population. We found variations in the values of diameters and IVCCI concerning the few studies performed in other pediatric populations, which highlights the importance of having specific reference values for different age groups in each population and opens the door to the possibility of generating more research in healthy children and even children with cardiac disorders. ■

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