The orthogonal measurements approach in estimating spleen size on CT images

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PURPOSE
We aimed to find out which single measurement and/or linear regression model correlates well with splenic volume using the orthogonal measurements approach.

METHODS
The study relied on retrospective analysis of 205 contrast-enhanced abdominal computed tomography (CT) examinations carried out in adult patients using a 320-detector CT system. CT volumetry was conducted by a semi-automated, model and threshold based segmentation algorithm that enables voxel-based volume calculation of abdominal organs. The orthogonal measurements were carried out in axial sections by measuring the maximum diameters of spleen projected in sagittal, coronal, and transverse planes. In addition, we calculated the diagonal diameter of spleen, which is a derivative of orthogonal measurements. Statistical analysis included calculation of interobserver agreement on orthogonal measurements, followed by model building using linear regression analysis of the measurements.

RESULTS
The interobserver agreement between two radiologists was very strong for all orthogonal measurements ($r \geq 0.971$). The highest model performance was detected with the diagonal diameter ($r^2=0.956$), followed by the superoinferior diameter ($r^2=0.857$). Agreement statistics revealed that the regression formula derived from the diagonal diameter outperformed that of superoinferior diameter.

CONCLUSION
The diagonal diameter appears to be the best parameter which correlates with splenic volume, whereas the superoinferior diameter can be an alternative in daily CT reporting practice. The orthogonal measurements approach not only provides a high interobserver agreement, but also the diagonal diameter can be translated into ultrasound studies.

A n accurate and reproducible assessment of spleen size is of utmost importance to determine the presence of splenomegaly, which serves as an important clinical finding in the diagnosis and follow-up of certain disease states such as parenchymal liver disease, liver congestion, infectious and inflammatory states, hematologic malignancies, infiltrative diseases, among others. Follow-up of spleen size is important in monitoring therapeutic response to the abovementioned disease states, especially if splenic rupture is a concern (1). Imaging studies have been the mainstay in estimating *in vivo* size of spleen, including ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI) (2). The sonographically detected maximum splenic length has long been used as an indicator of spleen size; however, it does not reflect variations in shape. Therefore, as a marker, it may be insufficient in borderline cases of splenomegaly, or in cases where a sensitive follow-up of spleen size is necessary. The same assumption holds true for other single unidimensional measurements obtained from CT or MRI, such as craniocaudal length of spleen.

Recently, with the advancement of liver transplantation surgery, CT volumetry of liver has become a standard technique for preoperative assessment of total and/or future remnant liver volume with an acceptable degree of error (3, 4). The updated versions of this

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technique use segmentation algorithms to detect the borders of liver and spleen on CT images, therefore, they can also be used to assess splenic volume (5). The disadvantages of the technique include radiation exposure during acquisition of CT images; and, as a postprocessing method, it is still cumbersome and time consuming in daily reporting practice. Therefore, researchers are still searching to develop surrogate markers of spleen size, which correlate well with splenic volume on cross-sectional images (6–11). These markers include: 1) single unidimensional nonorthogonal measurements of spleen, such as craniocaudal length, width or thickness; 2) calculations that use nonorthogonal measurements in a geometric formula such as that of an ellipsoid; and, 3) other formula-based calculations derived from regression analyses of the nonorthogonal measurements.

In this study, we have investigated the potential use of orthogonal measurements, rather than nonorthogonal measurements, as surrogate markers of splenic volume. This approach relies on measuring the maximum diameters of spleen projected in sagittal, coronal, and transverse planes. In addition, we have investigated the potential use of another parameter, the diagonal diameter of spleen, which is a derivative of orthogonal measurements. Linear regression models were built to identify the relationship between these measurements and reference splenic volumes. Our purpose is to find out which single measurement and/or linear regression model correlates well with splenic volume by using a standardized and reproducible method.

Methods

The study was approved by the institutional ethics committee. Written informed consent was waived by the Institutional Review Board.

Data selection

The study relied on retrospective analysis of 205 contrast-enhanced abdominal CT examinations of adult patients (63 females, 142 males; mean age, 38.4±15.1 years; range, 19–70 years), carried out between May 2017 and December 2017. Examinations were non-randomly collected from picture archiving and communication system (PACS) of our hospital using the following selection criteria: patients over 18 years old; images acquired during the portal phase; no motion artifacts that may interfere with unidimensional measurements and volumetric analysis; no lesions that may affect the splenic contours, such as mass lesions, post-traumatic changes, congenital and positional abnormalities. We used no clinical and laboratory data as selection criteria. Thus, considering the number of patients referred from Gastroenterology and Hematology clinics in our PACS, one can assume that number of the cases with a borderline and/or definitive splenomegaly, regardless of their criteria, are relatively higher when compared with the normative data from general population.

Image acquisition

All abdominal CT examinations were performed using a 320-detector CT system (Aquilion ONE, Toshiba Medical Systems). After patients were placed in the supine and feet first position on the couch, images were acquired in portal phase, i.e., 70 seconds after 80 mL of contrast agent was administered intravenously using a power injector (CT Motion, Ulrich GmbH and Co.) at a flow rate of 2.5 mL/s. Acquisiton parameters were: 80×0.5 mm detector collimation; 120 kV; 50–550 mA (with automatic modulation); 512×512 matrices; 1 mm section thickness; 0.8 mm section interval; and 10 as the noise index.

CT volumetry and definitions of measurements

After selection of the data, CT images were transferred to a post-processing workstation for CT volumetry and orthogonal measurements of the spleen.

CT volumetry was conducted by a semi-automated, model and threshold based segmentation algorithm that enables voxel-based volume calculation of abdominal organs in CT images (Vitrea software, Version 4.1.51, Vital Images). After the initial segmentation of the spleen, images were checked and manual corrections were applied when necessary.

All orthogonal measurements were carried out in axial sections by measuring the maximum diameters of the spleen projected in sagittal, coronal, and transverse planes. The diagonal diameter of the spleen was calculated as a derivative of the previous measurements by using the diagonal formula for a rectangular prism. See Table 1 and Fig. 1 for detailed definitions of the orthogonal planes and measurements.

Statistical analysis

Statistical analysis included calculation of interobserver agreement on orthogonal measurements, followed by model building using linear regression analysis. Interobserver agreement was evaluated by intraclass correlation coefficients between the data independently produced by two of the researchers (H.I., M.O.) in a randomly selected small subset of patients (n=35). The data included previously defined orthogonal measurements except formula-based calculation diagonal diameter. In the model building phase, ordinary least squares regression analyses were performed to obtain separate formulae for the superoinferior (SI), anteroposterior (AP), mediolateral (ML) diameters and the diagonal diameter of spleen in order to estimate splenic volume. A square root transformation was applied to volume to meet the linearity assumption. Significance of the regression model and coefficients were tested using t and F statistics, whereas Pearson correlation coefficient (r), coefficient of determination (r^2) and mean squared error statistics were used to assess the model adequacy. As an additional measure of model adequacy, studentized residuals were calculated for model diagnostics. To identify the best regression model, Akaike and Bayesian information criteria were calculated.

Finally, the best two models, as detected by comparison of coefficients of determination, were compared with each other. Passing-Bablok regression analyses were applied and Bland-Altman plots were constructed to assess whether a systematic error (constant or proportional) was present for each formula. Constant error was assumed to be present, if the confidence interval (CI) for the intercept did not contain the value 0. Besides, proportional error was assumed to be present, if the CI for the slope did not contain the value 1. Intraclass and concordance correlation coefficients

Table 1. The definitions of orthogonal planes and measurements

Orthogonal planes	Definition
Plane A	Midsagittal plane which divides vertebral body into two equal parts at the level of measurement
Plane B	Coronal plane which passes tangential to posterior border of vertebral body at the midline, and is perpendicular to Plane A at the level of measurement
Plane C	Transverse plane which passes through the axial section at which spleen first appears below the dome of diaphragm, and is perpendicular to Planes A and B
Orthogonal measurements	**Definition**
ML diameter	The difference between the vertical distances from Plane A to the most medial and the most lateral borders of spleen[a]
AP diameter	The sum of the vertical distances from Plane B to the most anterior and the most posterior borders of spleen[b]
SI diameter	The number of CT sections that include spleen multiplied by slice interval[c]
Derivative	**Definition**
Diagonal diameter	Square root of the sum of the squares of the ML, AP and SI diameters, i.e., $\sqrt{ML^2 + AP^2 + SI^2}$

ML, mediolateral; AP, anteroposterior; SI, superoinferior; CT, computed tomography.
[a]The most medial and lateral borders of the spleen do not have to be necessarily at the same axial level. [b]The most anterior and posterior borders of the spleen do not have to be necessarily at the same axial level. [c]Includes all spleen images starting from below the dome of diaphragm (Plane C) to the lowermost tip of spleen.

Table 2. Linear regression models using the SI, AP, ML diameters and their derivative, the diagonal diameter of spleen, in estimating splenic volume

Measurement	Regression model	Significance of model and coefficients			Measures of model adequacy			Model selection criteria	
		t_{β_0}	t_{β_1}	F	r	r^2	MSE	AIC	BIC
SI diameter	$\sqrt{Volume} = 9.112 + 0.656 \times \dfrac{SI^2}{1000}$	30.50**	34.74**	1206.54**	0.926**	0.857	2.36	932.58	942.53
AP diameter	$\sqrt{Volume} = 7.163 + 0.931 \times \dfrac{AP^2}{1000}$	13.63**	22.49**	505.88**	0.845**	0.715	3.32	1072.94	1082.89
ML diameter	$\sqrt{Volume} = 3.406 + 1.602 \times \dfrac{ML^2}{1000}$	2.90*	12.70**	161.215**	0.666**	0.444	4.64	1209.06	1219.02
Diagonal diameter	$\sqrt{Volume} = 3.406 + 1.602 \times \dfrac{ML^2}{1000}$	18.26**	66.06**	4363.35**	0.978**	0.956	1.31	692.68	702.64

* $P < 0.01$; ** $P < 0.001$.
SI, superoinferior; AP, anteroposterior; ML, mediolateral; r, Pearson correlation coefficient; r^2, coefficient of determination; MSE, mean squared error; AIC, Akaike information criteria; BIC, Bayesian information criteria.

(ICC, CCC) were calculated to test the agreement between the actual volume and the volume predicted by each formula. The calculated coefficients were interpreted as follows: 0–0.20 poor agreement; 0.21–0.40 weak agreement; 0.41–0.60 moderate agreement; 0.61–0.80 strong agreement; 0.81–1.00 very strong agreement. Analyses were conducted using TURCOSA Cloud (Turcosa Analytics Ltd Co) software. A P value less than 0.05 was considered as statistically significant.

Results

Based on the calculated intraclass correlation coefficients, the interobserver agreement between two radiologists was very strong for all orthogonal measurements, i.e., the ML diameter (r=0.971; 95% CI, 0.943–0.985), the AP diameter (r=0.971; 95% CI, 0.944–0.986), and the SI diameter (r=0.996; 95% CI, 0.992–0.998).

Ordinary least squares regression equations and model summaries built for orthogonal measurements are presented in Table 2. Correlation analysis between each orthogonal measurement and splenic volume revealed a positive, very strong and statistically significant correlation with the diagonal diameter (r=0.978, P < 0.05), the SI diameter (r=0.926, P < 0.05), and the AP diameter (r=0.845, P < 0.05), whereas a pos-

itive and strong correlation was present with the ML diameter (r=0.666, P < 0.05) after square root transformation. The estimated coefficients in the models built for each orthogonal measurement were found to be statistically significant (P < 0.05). With regard to the model performances for each measurement, the highest performance was detected with the diagonal diameter. The model using the diagonal diameter measurement explained the 95.6% of the variability of splenic volume, clearly outperforming the models built with other measurements (Fig. 2). As seen in scatter plot of the studentized residuals, most of the observations scatter between -2 and 2

Table 3. Passing-Bablok regression analysis and agreement statistics for the regression formula derived from diagonal and SI diameters

Measurement	Passing-Bablok regression		Agreement statistics	
	Intercept	Slope	ICC	CCC
Volume vs. regression formula derived from diagonal diameter				
Coefficient	11.21	0.97	0.992	0.985
95% CI	(-2.59–23.76)	(0.91–1.03)	(0.990–0.995)	(0.980–0.989)
Interpretation	No constant error	No proportional error	Perfect agreement	Perfect agreement
Volume vs. regression formula derived from SI diameter				
Coefficient	61.51	0.79	0.962	0.927
95% CI	(42.62–82.13)	(0.70–0.86)	(0.905–0.944)	(0.905–0.944)
Interpretation	Constant error is present	Proportional error is present	Perfect agreement	Perfect agreement

SI, superoinferior; ICC, intraclass correlation coefficient; CCC, concordance correlation coefficient; CI, confidence interval.
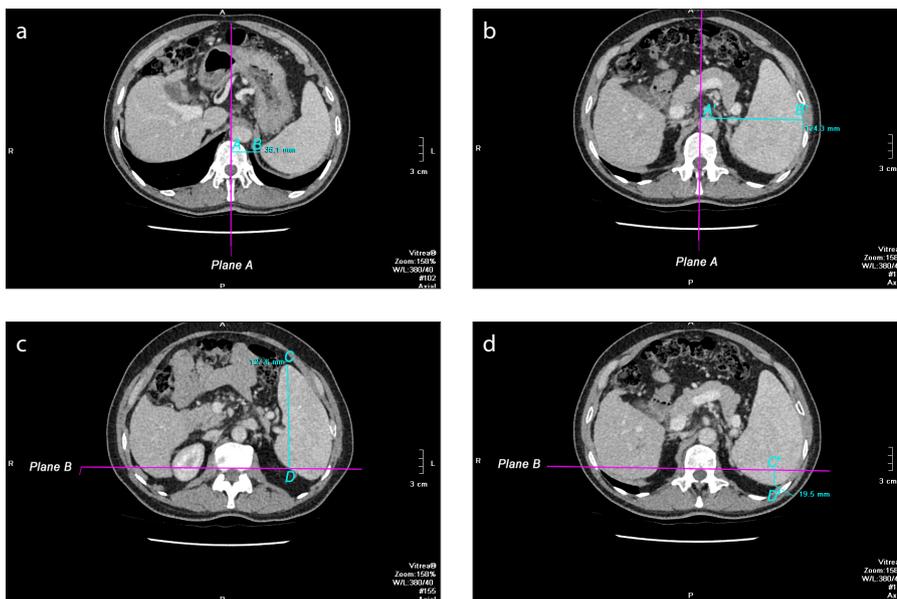

Figure 1. a–d. Axial sections showing the measurements of the mediolateral and the anteroposterior diameters. The mediolateral diameter is the difference between the vertical distances from midsagittal plane (Plane A) to the most medial **(a)** and the most lateral borders **(b)** of the spleen, i.e., it is the difference between the AB and A'B' lines in **(a)** and **(b)**, respectively. The anteroposterior diameter is the sum of the vertical distances from the coronal plane, which passes tangential to posterior border of vertebral body at the midline (Plane B) to the most anterior **(c)** and the most posterior borders **(d)** of the spleen, i.e., it is the sum of the CD and C'D' lines in **(c)** and **(d)**, respectively. Please note that in both measurements, the reference splenic borders do not have to be necessarily at the same axial level. Due to its definition, the SI diameter, which includes all spleen images starting from below the dome of diaphragm (Plane C) to the lowermost tip of the spleen, is not included in the image. For detailed definition of the planes and the measurements, please see Table 1.

levels and distributed randomly around the 0 value (Fig. 3).

Table 3 shows the results of the Passing-Bablok regression analysis and the agreement statistics based on the actual spleen size and predictions obtained from the best two models, i.e., the model derived from the diagonal diameter (r^2=0.956) vs. the SI diameter (r^2=0.857). Agreement sta-tistics revealed that both the regression formula derived from the diagonal diameter and the SI diameter had perfect agreement with the actual splenic volume; however, regression formula derived from the diagonal diameter had the highest agreement statistics (ICC=0.992, CCC=0.972) and outperformed the formula derived from SI diameter. When we looked at the Passing-Bablok regression analysis results, both constant and proportional error were present in the formula derived from SI diameter, whereas no systematic error was detected in formula derived from diagonal diameter. Bland-Altman plots supported our findings (Fig. 4). A positive trend in Fig. 3b displays the systematic error of the SI diameter derived regression formula.

Discussion

The aim of this study was to find out which single measurement and/or linear regression model correlates well with splenic volume using the orthogonal measurements approach. Correlation coefficients derived from linear regression analysis showed that the best orthogonal measurements that could be used as a surrogate marker for splenic volume are the diagonal diameter (r=0.978), followed by the SI diameter (r=0.857). Therefore, the best regression formulas in estimating splenic volume were the formula derived from the diagonal diameter, followed by the formula derived from the SI diameter. Agreement statistics revealed that the regression formula derived from the diagonal diameter clearly outperformed the other with no systematic error. Since calculation of the diagonal diameter is relatively cumbersome, requiring measurements in all orthogonal planes, the SI diameter can be an alternative in CT reporting practice. Some of the previous researchers have produced similiar results indicating that craniocaudal length of the spleen correlates well with the splenic volume (7, 8, 11). However, other studies advocate using splenic width as the
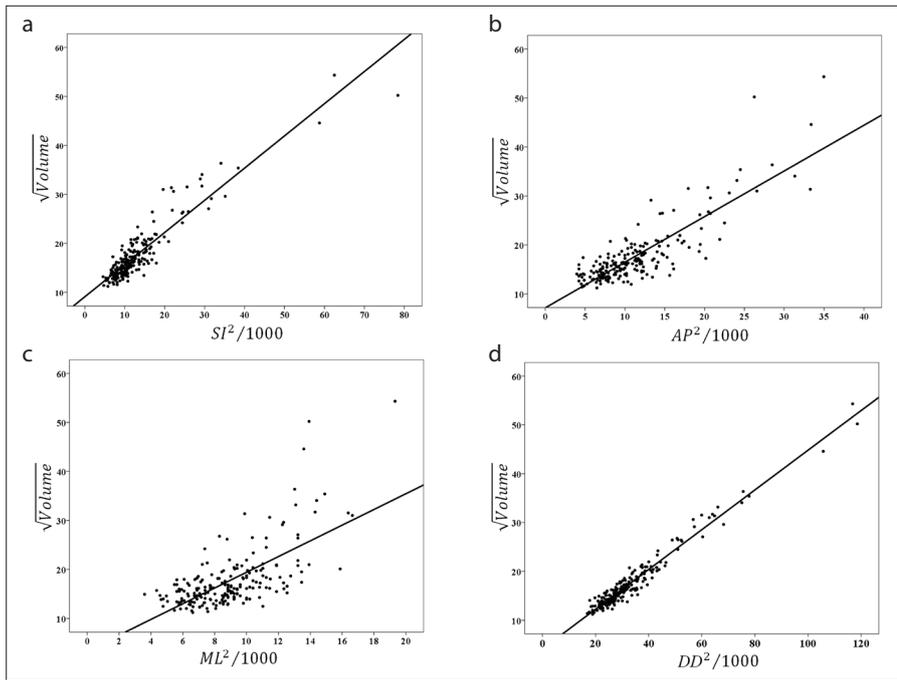
Figure 2. a–d. Scatter plots showing the model performances for each measurement. The highest performance was detected with the diagonal diameter. SI, superoinferior diameter; AP, anteroposterior diameter; ML, mediolateral diameter; DD, diagonal diamater.
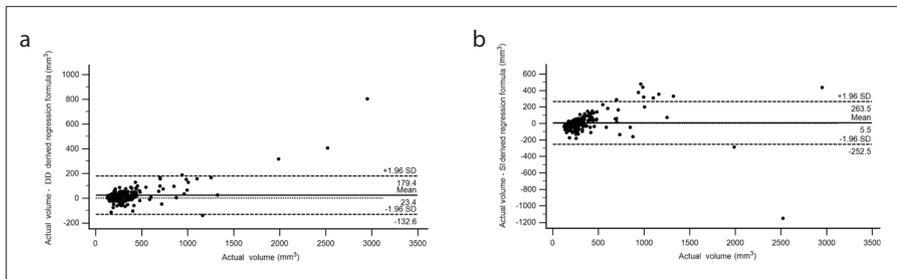

Figure 4. a, b. Bland-Altman plots based on the actual spleen size and predictions obtained from the model derived from the diagonal diameter **(a)** and the SI diameter **(b)**. A positive trend in **(b)** displays the systematic error of the regression formula derived from the SI diameter. SI, superoinferior diameter; DD, diagonal diameter.

Figure 3. Scatter plot of studentized residuals of the data. Most of the observations scatter between -2 and 2 levels and are distributed randomly around the 0 value.

As a future project, we would like to list our stepwise recommendations as follows: first, since this is a single center study, our findings need to be externally validated. Second, the diagonal diameter detected on CT images should be correlated with the sonographically detected maximum splenic length to confirm the interchangeability of both data. Finally, if the historical value of sonographically detected maximum splenic length is confirmed in the previous step, this measurement can be used to establish population-specific normative data with regard to age, sex, body weight and length, because US provides a radiation-free examination, which is suitable for large series of patients.

Our study has the following limitations: first, the study population is confined to adult patients; second, it is necessary to validate our findings in cases with splenic enlargement; however, to accomplish this, there should be consensus on an accurate and reproducible method of measurement, which correlates well with spleen size, so that upper limits of the normative data can be determined to conclude on splenomegaly. Third, the number of patients included interobserver agreement study is limited, but since the agreement between radiologists was very strong for all orthogonal measurements, we believe that it is sufficient to reach a conclusion. Fourth, the proposed method can be used in patients who had already undergone CT examination; however, in other patient groups and in patients whom follow-up of spleen size is necessary, it is not feasible due to serial radiation exposure.

In conclusion, based on abdominal CT examinations of adult patients, our study revealed that the diagonal diameter is the

best parameter (6, 9, 10). The reason behind the conflict may be lack of a consensus on how to define the nonorthogonal planes of measurement: readers should notice that the SI diameter in this study, which roughly corresponds to craniocaudal length in other studies, is measured in axial planes by counting all spleen images starting from below the dome of diaphragm to the lowermost tip, not necessarily involving the medial tip of spleen in the same coronal plane. Similarly, splenic borders used in measurement of the ML and AP diameters do not have to be necessarily at the same axial level.

How do these findings influence our practice? In our view, the orthogonal measurements approach offers two main advantages: first of all, it provides a high interobserver agreement in measurements since their definitions are dependent on orthogonal planes of reference, rather than vague planes. This leads to reproducible measurements which can be reliably used. To our knowledge, there is no single study investigating the interobserver agreement on CT-based nonorthogonal measurements. Second, the diagonal diameter calculated from CT images can be translated into US studies, since, geometrically, this measurement corresponds to the maximum splenic length detected on US. If it is proven that a strong correlation exists between both measurements, they can be used interchangeably in initial diagnosis and follow-up of splenomegaly.
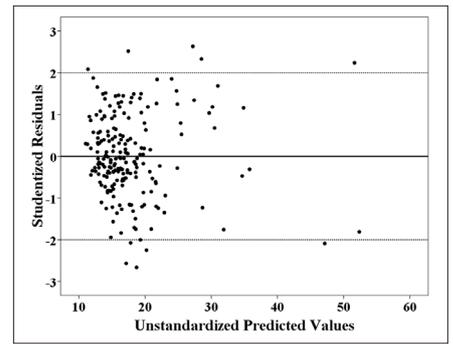
best parameter to use as a surrogate marker for splenic volume. In daily CT reporting practice, the SI diameter can be an alternative to the diagonal diameter due to the ease in measurement. The orthogonal measurements approach in this study not only provides a high interobserver agreement, but the diagonal diameter calculated from CT images can be translated into US studies, which can be used in establishing normative data in large series of patients.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Chow KU, Luxembourg B, Seifried E, Bonig H. Spleen size is significantly influenced by body height and sex: establishment of normal values for spleen size at US with a cohort of 1200 healthy individuals. Radiology 2016; 279:306–313. [CrossRef]

2. Brant WE. Pancreas and spleen. In: Brant WE, Helms CA. ed. Fundamentals of diagnostic radiology. 4th ed. Philadelphia: Lippincott, Williams and Wilkins, 2012; 720–733.

3. Lodewick TM, Arnoldussen CW, Lahaye MJ, et al. Fast and accurate liver volumetry prior to hepatectomy. HPB (Oxford) 2016; 18:764–772. [CrossRef]

4. D'Onofrio M, De Robertis R, Demozzi E, Crosara S, Canestrini S, Pozzi Mucelli R. Liver volumetry: Is imaging reliable? Personal experience and review of the literature. World J Radiol 2014; 6:62–71. [CrossRef]

5. Pattanayak P, Turkbey EB, Summers RM. Comparative evaluation of three software packages for liver and spleen segmentation and volumetry. Acad Radiol 2017; 24:831–839. [CrossRef]

6. Prassopoulos P, Cavouras D. CT assessment of normal splenic size in children. Acta Radiol 1994; 35:152–154. [CrossRef]

7. Bezerra AS, D'Ippolito G, Faintuch S, Szejnfeld J, Ahmed M. Determination of splenomegaly by CT: is there a place for a single measurement? AJR Am J Roentgenol 2005; 184:1510–1513. [CrossRef]

8. Prassopoulos P, Daskalogiannaki M, Raissaki M, Hatjidakis A, Gourtsoyiannis N. Determination of normal splenic volume on computed tomography in relation to age, gender and body habitus. Eur Radiol 1997; 7:246–248. [CrossRef]

9. Joiner BJ, Simpson AL, Leal JN, D'Angelica MI, Do RK. Assessing splenic enlargement on CT by unidimensional measurement changes in patients with colorectal liver metastases. Abdom Imaging 2015; 40:2338–2344. [CrossRef]

10. Nuffer Z, Marini T, Rupasov A, Kwak S, Bhatt S. The best single measurement for assessing splenomegaly in patients with cirrhotic liver morphology. Acad Radiol 2017; 24:1510–1516. [CrossRef]

11. Kucybala I, Ciuk S, Tęczar J. Spleen enlargement assessment using computed tomography: which coefficient correlates the strongest with the real volume of the spleen? Abdom Radiol 2018; 43:2455–2461. [CrossRef]