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Possible Anthropometric Explanation of Age-related Changes in Splenic Volume in a Sample of Healthy Iraqi Individuals Using Ultrasonography

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Abstract

Background Spleen is a hemopoietic organ which is capable of supporting elements of different systems. Determination of spleen size is important in diagnosing small, normal or enlarged spleens. Songraphy can rapidly and reliably help to determine the size of the spleen.

Objective The purpose of this study was to analyze the changes in splenic volume with respect to age using anthropometric measurents (body mass index (BMI), body surface area (BSA)) and to find the predicting equation of spleen volume.

Methods 215 Iraqi subjects (103 females with age range (6-74) years and 112 males with age range (7-75) years) without conditions that can affect the spleen or splenic abnormalities were evaluated with ultrasonography. Spleen length, width and thickness were measured and spleen volume was calculated. Spleen size was correlated with age, gender, BMI and BSA.

Results The mean splenic volume was significantly variable in different age groups.The spleen volume increases starting from childhood to reach a peak in a young adults (20-49) years and then declines in the middle age and elderly subjects (age with greater than 50 years). Splenic volume for males was significantly higher than females. BSA had a stronger linear correlation with splenic volume than BMI. Multiple regression analysis indicated that BSA had significant positive association with spleen volume in subjects younger than 50 years.

Conclusion Spleen volume was significantly variable among different age groups. Spleen volume affected by BSA especially in subjects younger than 50 years. These results illustrate that the normal value of spleen volume affected by different factors 1) age 2) sex 3) BMI 4) BSA.

Key words Spleen volume, Ultrasonography, Age, BMI, BSA

Introduction

The spleen is an intra abdominal organ; many diseases can affect its size ranging from infective processes to malignant disorders. Spleen size varies widely according to age. The estimation of splenic size in vivo is often important in the diagnosis, treatment and prognosis of a variety of disorders. Palpation and percussion are the standard bedside techniques to document spleen size, but are far from accurate to detect small increase in size [(1)]. The spleen has to be enlarged two to three times its normal to be clinically palpable [(2,3)]. Therefore the imaging has become essential for the accurate measurement of the splenic size, the serial monitoring of the splenic size over the

course of the patients illness and development of the guidelines for return to play. Several prior studies have sought to develop the standards for the splenic size such as Computed Tomography scan, Scintigraphy, Magnetic Resonance Image and Sonography. The conventional sonography was found to be a well-established, widely used relatively inexpensive mean of assessing the splenic size without ionizing radiation. Radiography expose patient to x-ray and radionuclide studies expose the patient to gamma radiation [2,4-6]. Sonography is routinely used to determine the internal structure of the body because the examination is real time, independent of organ function and no risk of ionizing radiation. Ultrasonography is a non-invasive, established, safe, quick and accurate method for the measurement of spleen size [6]. It allows a physician to see inside a patient without resorting to surgery. Several published studies have examined the range of spleen dimensions and volume in normal adults and their correlation with age, gender and body habitus [7-11].

The present study was designed to measure three dimensional ultrasonography of the spleen in healthy Iraqi subjects of different age group and correlates them with the anthropometric body mass index (BMI) and body surface area (BSA) measurement.

Methods

Spleen measurements were performed for 215 individuals prospectively recruited from individuals referred for US at Al-Kadhimiya Teaching Hospital for the period March 2009 to March 2010. The exclusion criteria were recent febrile illness (within the last 6 months), upper abdominal symptoms, liver disease, history of splenectomy, malignancy, malaria or sickle cell anaemia or trait, and those whose examination showed focal splenic lesions. Pregnant females were also excluded as spleen size has been shown increase during pregnancy [12].

All examination were performed by same radiologist experienced in abdominal US using a commercially available real time US scanner Siemen sonoline versa Pro with a 3.5-5 MHz sector transducer.

Images were obtained with the subject lying in the supine or slightly right lateral decbitus position, and through an oblique intercostal approach. Following suspended deep inspiration all measurements were made on images through the splenic hilum using electronic calipers .In each examination, three sequential measurements of the splenic length, thickness and width were obtained, and the mean value of each dimension was recorded to ensure minimal intraobserver variation. All measurements were recorded to the nearest millimeter.

Maximal splenic length was defined as the maximum distance between the most superior margin and inferior margin of the spleen on a longitudinal coronal sonogram. Maximal splenic thickness was defined as the maximal distance between the medial and lateral borders of the spleen on a transverse sonogram. Maximal splenic width was defined as the maximal anterior to posterior diameter of the spleen on a transverse sonogram [13].

Spleen volume was determined for each subject according to the formula for a prolated ellipse (0.524×width×thickness×length), which has been shown to be an accurate method for the calculation of spleen volume [14-16]. Height and weight were obtained to calculate the body mass index kg/m^2. Subjects were categorized into three groups; Group I (first quartile) consisted of subjects with BMI of ≤ 23.1 kg/m^2, group II (interquartile) subjects with BMI of (23.2-27.9) kg/ m^2 and group III (fourth quartile) subjects with BMI of ≥ 28 kg/m^2. Body surface area (BSA) was obtained based on the formula of Dubois [17].

BSA= ($W^{0.425}$×$H^{0.725}$) ×0.007184 where W=weight in kg, H=height in cm, factor unit =cm/kg. Subjects were categorized into three group .group I (first quartile consisted of subjects with BSA of ≤ 1.68 m^2), group II (inter quartile) subjects with BSA of (1.69 -1.93) m^2 and group III (fourth quartile) were individuals BSA ≥ 1.94 m^2.

Statistical Analysis

Analysis was done by using the statistical package for social sciences (SPSS) version 13 software. The mean difference between the two groups was assessed for statistical significance by independent samples t-test. Bivariate correlation was performed calculating Pearsons linear correlation coefficient to assess the direction strength and statistical significance of linear correlation between two quantitative variables. Analysis of variance (ANOVA) was used to test for differences in the mean of outcome variables between more than two groups. The 95% confidence interval for mean was used to predict the mean in reference population with 95% confidence. Multiple linear regression model was used to assess the independent association of a set of explanatory variables on a quantitative outcome variable. $p< 0.05$ was considered statistically significant.

Results

The study included 215 healthy subjects (103 females with mean age 37.4 years (range 6-74) years and 112 males with mean age 37.3 years, (range 7-75) years). The spleen length, height and width of them as shown in table 1.

Table 1. Splenic dimensions (length, height & width) in the studied group

Dimension	Females N = 103			Males N = 112			Total N = 215		
	mean±SD	Range	SE	mean±SD	Range	SE	mean±SD	Range	SE
Splenic length	10.6±1	7-12.6	0.1	11.2±1	6.7-12.9	0.1	10.9±1.1	6.7-12.9	0.07
Splenic height	4.9±0.7	3.1-6.8	0.07	5.4±0.8	2.8-7.8	0.08	5.1±0.8	2.8-7.8	0.06
Splenic width	4.1±0.5	2.8-5	0.05	4.5±0.6	2.6-5.9	0.05	4.3±0.6	2.6-5.9	0.04
Splenic volume	115.8±34.2	35.9-210.4	3.37	143.7±41.1	27.4-248.9	3.89	130.3±40.4	27.4-248.9	2.75

Splenic length, height, and width measured in cm. Splenic volume measured in cm^3

Splenic volume correlates in a curve linear fashion to age. It was shown to increase starting from childhood to reach a peak in a young adults (20-49 years) and then decline in middle age and elderly subjects(age with greater than 50 years). Figure 1 shows that quadratic, cubic model provided the best fit for the observed data.

The mean of splenic volume was significantly variable in different age groups.Splenic volume for males was significantly higher (143.7 cm^3) than females (115.8 cm^3) as shown in table 2.

Table 2. Correlations between splenic volume, age and gender

Character		Spleen volume (cm^3)			
		No.	Range	mean±SE	Mean±1.96SD (95% CI)
Age (years)	≤ 10	6	27.4-64.7	45.5±6.16	15.9 to 75.1
	11-20	18	59-152.7	107.4±7.37	46.1 to 168.7
	21-30	42	77.6-185.8	127.4±4.1	75.3 to 179.5
	31-40	71	69.2-248.9	139.7±4.68	62.5 to 216.9
	41-50	41	48.3-245.2	148.1±6.59	65.4 to 230.8
	51-60	118	63.5-192.8	123.9±8.13	56.3 to 191.5
	61-70	13	61.1-174.6	122.5±10.58	47.6 to 197.4
	≥71	6	70.1-154.6	107.2±15.35	33.5 to 180.9
Gender	Female	103	35.9-210.4	115.8±3.37	48.8 to 182.8
	Male	112	27.4-248.9	143.7±3.89	63.1 to 224.3

P = <0.001 (ANOVA) for age, P = <0.001 (t-test) for gender

To study the changes in splenic volume for males and females separately, we grouped the readings to three important age groups: (< 20, 20-49, and ≥50). We see a growing in splenic volume for teenagers (age < 20 years), the volume remains same in size as a plateau for young adults (age between 20-49 years) then, the splenic volume decline in elderly group (age ≥50 years) (Figure 2).

Table 3 shows that the mean of spleen volume has a significant increases as BMI increase from ≤ 23.1 to greater than 28 kg/m^2 (p=0.001) and higher significant increase with the BSA from ≤ 1.68 to greater than 1.9 m^2 (p<0.001); this is more illustrated with correlation to sex of patient. The BSA had a slightly stronger linear correlation with splenic volume than BMI in males and females (r=0.574, p<0.001 for females; r=0.5, p<0.001 for males).

Table 3. Correlations between spleen volume, BMI and BSA

Parameter		Spleen volume (cm^3)			
		No.	Range	Mean±SD	SE
BMI (kg/m^2)	First quartile (≤ 23.1)	57	27.4-219.7	117.7±41.3	5.47
	Interquartile range (23.2 - 27.9)	105	59-241.8	129.6±36.9	3.6
	Fourth quartile (≥28.0)	53	77.6-248.9	145.2±41.8	5.74
BSA (m^2)	First quartile (≤1.68)	54	27.4-174	99.2±33.9	4.62
	Interquartile range (1.69 - 1.93)	108	63.5-241.8	135.4±31.7	3.05
	Fourth quartile (≥1.94)	53	69.2-248.9	151.7±44	6.04

BMI: body mass index, BSA: body surface area, for BMI (r=0.35, p<0.001 for females; r=0.32, p<0.001 for males}, for BSA {r=0.574, p<0.001 for females; r=0.5, p<0.001 for males); ANOVA p=0.001 for BMI, p<0.001 for BSA

As shown in table 4 part A, age had the strongest independent association with the spleen volume in age group less than 20 years. The spleen volume is expected to increase by 7 cm^3 for each year after adjusted for gender .Male had significantly higher spleen volume by about 25.9 cm^3 as compared to females after adjusting the age in age group less than 20 years .The overall model was statistically significant and able to explain 71% of variation and cause variable, we had found regression equation which formulated as spleen volume (cm^3) = -21.3+ (7×age) + (25.9×gender).

Gender was the most important variable in explaining changes in spleen volume in age group between 20-49 years. Males had significantly higher in spleen volume by about 26.3 cm^3 as compared to females after adjusting age. Age is associated with a statistically significant increase in spleen volume in age group between 20-49 years, for each year; the spleen volume is expected to increase by about 1.1 cm^3 after adjusting for gender. The overall model was statistically significant & able to explain 17% of variation &cause variable, we had found regression equation which formulated as spleen volume (cm^3) = 87.5 + (1.1×age) + (26.3×gender) (Table 4 part B).

As shown in table 4 part C, male gender is associated with a statistically significant increase in spleen volume by 36.3 cm^3 compared to females at age group ≥50 years after adjusting age. Age is associated with a statistically significant decrease in spleen volume, for each one year increase in age, the spleen volume expected to decrease by 1.4 cm^3 after adjusting the gender. The overall model was statistically significant & able to explain 33% of variation and cause variable, we had found regression equation which formulated as spleen volume (cm^3) = 187.9+ (-1.4×age) + (36.3 ×gender).

Table 4. Multiple liner regression models with spleen volume as the dependent (response) variable and age and gender as independent (explanatory) variables (stratified by age group)

	Age Group (Years)	Partial regression coefficient	Standardized coefficient	P value
(A) <20	Constant	-21.3		0.22
	Age in years	7	0.748	<0.001
	Male compared to female	25.9	0.334	0.014
P (Model) <0.001, R2 = 0.71				
Regression equation: spleen volume = -21.3+(7×age)+(25.9×gender) (where male gender =1 and female gender =0)				
(B) 20-49	Constant	87.5		<0.001
	Age in years	1.1	0.204	0.007
	Male compared to female	26.3	0.35	<0.001
P (Model) <0.001, R2 = 0.17				
Regression equation: spleen volume = 87.5 +(1.1×age)+(26.3×gender) (where male gender =1 and female gender =0)				
(C) ≥ 50	Constant	187.9		<0.001
	Age in years	-1.4	-0.308	0.03
	Male compared to female	36.3	0.511	0.001
P (Model) <0.001, R2 = 0.33				
Regression equation: spleen volume = 187.9+(-1.4×age)+(36.3 ×gender) (where male gender =1 and female gender =0)				

Body surface area had the strongest independent association with the spleen volume at age group less than 20 years old, for each one square meter increase in body surface area, the spleen volume increase by about 67.6 cm^3 at age group less than 20 years old after adjusting the age, gender and BMI. Male gender is associated with a statistically significant increase in spleen volume by about 20.5 cm^3 compared to female after adjusting the age and anthropometry measurements (BMI and BSA). BMI was statistically significant increase in spleen volume at age <20 years. For each one kg/m^2 increase in BMI, the spleen volume is expected to increase by 2.7 cm^3 after adjusting the age, gender and BSA as shown in table 5 part A. The overall model was statistically significant and able to explain 82% of variation and cause variable, we had found regression equation which formulated as spleen volume (cm^3) = -101.1 + (1.6×age)+ (20.5×gender)+(2.7× BMI)+(67.7×BSA).

In table 5 part B, BSA had the strongest independent association with the spleen volume at age group between 20-49 years. For each 1 m^2 increase in BSA, the spleen volume expected to increase by 70.9 cm^3 after adjusting the age, gender and BMI. Male gender is associated with a statistically significant increase in spleen volume by about 18 cm^3 compared to female after adjusting the age and anthropometric measurements the overall model was statistically significant and able to explain 27% of variation and cause variable, we had found regression equation which formulated as spleen volume (cm^3) = -37.8 + (0.7×age) + (18×gender) + (0.5× BMI)+(70.9×BSA).

Male gender is associated with a statistically significant increase in spleen volume by about 37 cm^3 compared to female at age group ≥50 years after adjusting the age and anthropometric measurements. Splenic volume decreased at age group ≥ 50 years (statistically not significant). BMI and BSA had no effect or statistically significant association with spleen volume when used in a multivariation model, we had found regression equation which formulated as spleen volume (cm^3)=165.1+(-1.3×age)+(37×gender)+(0.8×BMI)+(-3.2×BSA),table 5 part C.

Table 5. Multiple linear regression models with spleen volume as the dependent (response) variable and age, gender, BMI and BSA as independent (explanatory) variables (stratified by age group)

Age Group (Years)		Partial regression coefficient	Standardized coefficient	P value
(A) <20	Constant	-101.1		0.004
	Age in years	1.6	0.173	0.51
	Male compared to female	20.5	0.264	0.026
	BMI (kg/m^2)	2.7	0.256	0.038
	Body surface area (m^2)	67.7	0.55	0.044
P (Model) <0.001, R2 = 0.82				
Regression equation :spleen volume = -101.1+(1.6×age)+(20.5×gender)+(2.7× BMI)+(67.7×BSA) where male gender =1 and female gender =0				
(B) 0-49	Constant	-37.8		0.24
	Age in years	0.7	0.131	0.07
	Male compared to female	18	0.239	0.003
	BMI (kg/m^2)	0.5	0.062	0.48
	Body surface area (m^2)	70.9	0.306	0.001
P (Model) <0.001, R2=0.27				
Regression equation :spleen volume = -37.8+(0.7×age)+(18×gender)+(0.5× BMI)+(70.9×BSA) where male gender =1 and female gender =0				
(C) ≥ 50	Constant	165.1		0.09
	Age in years	-1.3	-0.279	0.1
	Male compared to female	37	0.52	0.003
	BMI (kg/m^2)	0.8	0.066	0.73
	Body surface area (m^2)	-3.2	-0.014	0.94
P (Model) =0.007, R2=0.33				
Regression equation :spleen volume = 165.1+(-1.3×age)+(37×gender)+(0.8× BMI)+(-3.2×BSA) where male gender =1 and female gender =0				

Discussion

The spleen is a large organ to the left of the stomach and below the diaphragm, serving to store blood, disintegrate old blood cells, filter foreign substances from the blood, and produce lymphocytes (white blood cells). In this study, we analyzed the changes in splenic volume with age using anthropometric measurement (BMI and BSA).

As shown in the results of this study, there is a significant increase in splenic volume from childhood and teenager to middle age and significant decrease at older age among all these subjects in both sexes. These results were in agreement with a previous study [18] where the splenic length and width of both sexes increases linearly with age until the middle age with a maximum of 12 cm, and thereafter undergoes gradual diminution, and a phenomena documented by Bisset et al [19]. Sharkawy et al [20] found all the measured parameters increased with age till 20 years. Previously reported [21] showed a rapid growth in splenic length up to age 20 years, followed by a mild decrease. Some authors showed a decrease in spleen diameter with increasing age [7,11] as well as the study of Arore et al [22] showed that the splenic length, width and thickness decreased with increased age in both males and females. Hoefs et al [23] found a linear correlation of splenic volume with

age and suggested formula. The results of our study partly agreed with the study of Adil et al [24] who found that a splenic volume also moderately correlated with age. While other studies [8,13] found no correlation of spleen size with the age of the subjects.

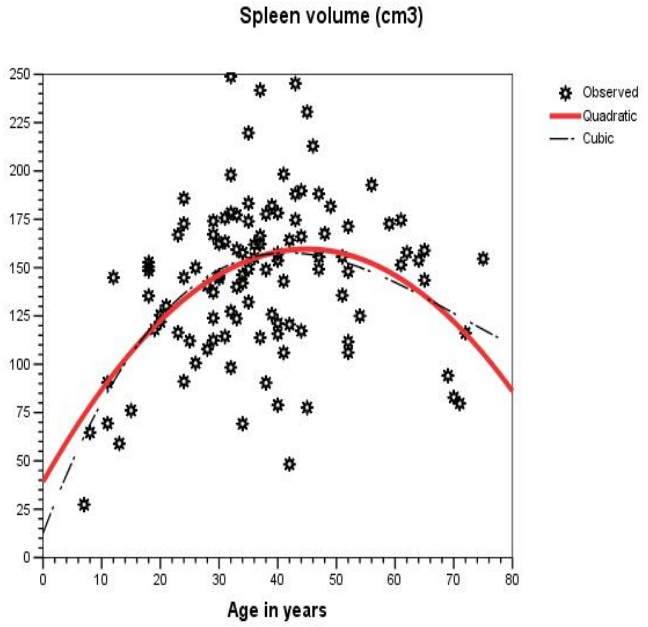

Figure 1. Correlation between the splenic volume and age

In the current study spleen volume is found to be larger in males than in females .The results come in concordance with some studies [10,25-28]. Results of a previous study [10] found statistical significant differences between male and female subjects from about 15-40 years with spleen of males being about 0.5 cm longer. Perhaps this may be due to the differences in height, weight, surface area and the genetic factors. This was different when compared with findings of prassopulos et al [9], kanekoj et al [11], Elsharkawy et al [20], Hoefs et al [23] and Ramak [29]. They observed that there are no differences in spleen size between genders.

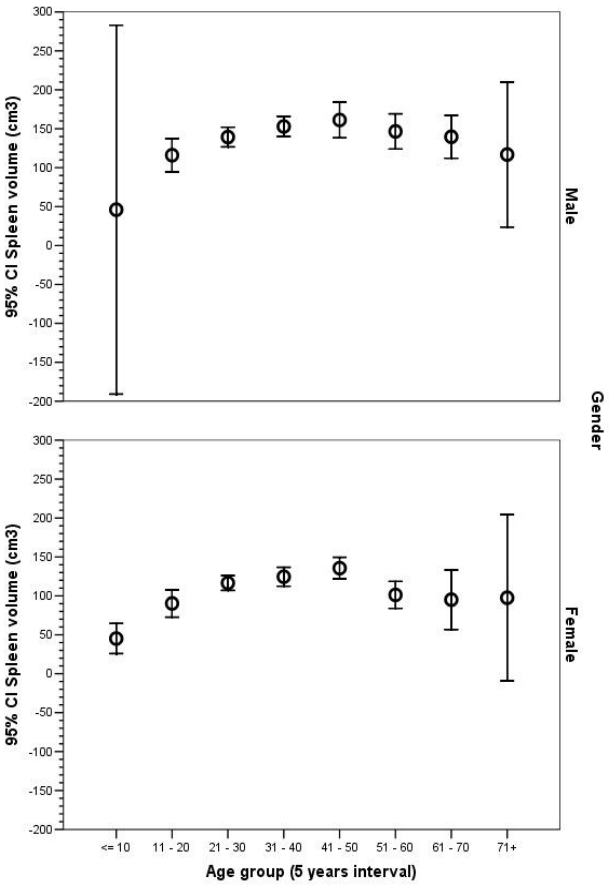

Figure 2. The splenic volume by age after controlling for gender.

Body surface area is a function of both height and weight either of which may vary separately. The results of our study showed that BSA had the strongest independent association with the spleen volume in subjects younger than 50 years, BMI showed statistically significant positive association with spleen volume at age <20 years .The relationship between spleen volume, BMI and BSA has been reported in literature [30]. The splenic volume correlated with BMI and BSA. The formulae spleen volume =BSA [278 *age (-0.36)] was derived and can be used to estimate the splenic volume. Spleen volume shows a strong correlation to its length as reported by previous studies [31,32]. Therefore spleen volume can be replaced its length deduction reasoning. Results in a prior study [33] found that the spleen length was highly

correlated with BSA. Multiple regression analysis indicated that BSA had significant positive association with spleen length in a sample with age range 1 day-17 years. This strong relationship between spleen volume and BSA is not surprising because for may be physiologic & clinical purposes and BSA is a better indicator of metabolic mass than body weight because its less associate with excessive body fat. On the other hand a study of Mustapha et al [13] didn't find a significant correlation between BMI and spleen volume, other study found the spleen volume was no significantly correlated with BSA [25]. This may be due to nutritional factors or environmental factors.

There were few limitations in this study. **First**, although depending on the use of a single investigator and the same equipment to perform the measurements in all the participants to increase the reproducibility (reliability) we were unable to assess interobserver variability .We used the mean of three measurements for each of the spleen parameters investigated to mitigate concerns about reproducibility and intraobserver variability. In one study, the mean splenic length measurements were shown to have a higher reproducibility than maximal splenic length measurements [34]. It would be more ideal if two observers were included which would allow the calculation of an interobserver error.

second we used the formula for a prolated ellipse to calculated the spleen volume as it is widely accepted in the published literature for the estimation of volume from unidimensional measurements .However, its recognized that the spleen can often be irregularly shaped, and the estimated volume using this formula is less accurate nevertheless, its wide use in the published literature allows us to perform meaningful comparison with our data.

In conclusion, splenic volume was significantly variable in different age groups. We see a growing in splenic volume in teenager (age <20 years), the splenic volume remain in the same size as a plateau in young adult (age between 20-49 years) then, the splenic volume decline in elderly group (age with greater than 50 years). Splenic volume for males was significantly higher than females. BSA had a significant positive association with spleen volume in subjects younger than 50 years. These results illustrate that the normal value of spleen volume affected by different factors 1) age 2) sex 3) BMI 4) BSA.

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