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Application of Stereology in Liver Volume Measurements Using Computed Tomography Scan

Aplicación de la Estereología en Mediciones de Volumen Hepático Mediante Tomografía Computarizada

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SUMMARY: The application of stereology in hepatobiliary conditions is essential in liver volume estimation. Computerized topographic scan with contrast is a reliable method in liver scanning for precise boundaries demarcation. Liver volumetry varies in relation to different factors. Reports showed a correlation of liver volume with sex and body mass index. Steady relation between age and ethnicity is not established. This study aimed to design a protocol for liver volume measurement and apply it in the estimation of volume among the Sudanese population use stereology. Recruitment of the study population was obtained in the royal scan clinic in Khartoum by making an announcement for participation in the study. Patients with a history of hepatobiliary diseases were excluded. CT abdomen with contrast was obtained in DICOM format and transferred to computer-based software for image analysis. A protocol was designed and validated and then applied in volume estimation using software MRIcro for image display, ImageJ for volume estimation, and Onis 2.6 as image viewer. 300 apparently healthy volunteers were recruited. The protocol reliability result was 0.805. Absolute mean liver volume was 3261.32 ± 1365.313 cm^3. High liver volume among females was detected than among males. A positive correlation was detected between volume and body mass index (p-value 0.001) regardless of sex. Relation with age showed a rough steady rise till the age of 50 years then it started to decline steadily. The relationship was detected in liver volume with sex and body mass index. More studies are needed to investigate the relationship between ethnicity and age groups.

KEY WORDS: Liver volumetry; Liver transplantation; CT scan with contrast; Stereology; planimetry technique.

INTRODUCTION

Precise liver volume assessment is essential in many conditions in hepatology. Determination of appropriate graft sizes in living-related liver transplantation for patients with end-stage liver failure is essential (Duran *et al*., 2007). It is also important in volume evaluation for follow up after partial hepatectomy, and in assessing the prognosis in liver mass (Kubota *et al*., 1997). The selection of the suitable scanning technique is a key factor in volumetry. Computerized Tomography (CT) with contrast is proved to be superior to Magnetic Resonance Imaging (MRI) in liver scanning for the clear demarcation of liver boundaries. The image is then processed in computer-based software for image analysis to obtain volume (Saylisoy *et al*., 2005; Childs *et al*., 2015). The automated liver extraction schemes for measuring liver volume showed accurate results when compared with the manual methods (Suzuki *et al*., 2011). Computation of volumetry is obtained through stereology which is the science of obtaining three-dimensional data out of two-dimensional images. It is applied in organs of irregular shape and dimensions as it provides reliable data compared with conventional procedures (Weibel *et al*., 1966; Sundberg, 1992; Marcos *et al*., 2012). Different stereological techniques are used in volume measurement. One of these methods is planimetry in which liver boundaries are demarcated by manual or automatic techniques then the volume is computed (Altunkaynak *et al*., 2012). This study aimed to apply stereology in the determination of liver volume among the Sudanese population using the planimetry technique.

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MATERIAL AND METHOD

This is a cross-sectional descriptive study done between September 2015 to March 2017 in Royal Scan Clinic, Khartoum, Sudan. The clinic is considered as a referral center for different types of scanning including CT scanning with contrast. The announcement to participate in the study was set in the CT section. The selected participants were those patients who come for abdomen CT with contrast and they have no suspicion of liver problems. Consent was obtained after informing the candidates that acceptance or rejection to participate will not affect the type and level of the offered service. Exclusion criteria were the presence of a history of hepatobiliary disease and contraindication to contrast. The scan was performed using a Toshiba Aquilion™ 64 slices scanner (Toshiba Medical Systems, Nasu, Japan) – version 3.0 software. Omnipaque contrast in a dose of 15 - 20 mL given orally in 1 liter of water through 60 to 90 minutes and 200 mL to be taken at scanning time. During scanning an IV vial of omnipaque contrast was given by automatic injector in a dose of 1 mL/kg at a rate of 4 to 5 mL per second. The patient was placed for scanning in a shoulder-first position with extended shoulders. Arterial and venous phases were reported and after a delay of 5 minutes, another scan was taken to exclude liver pathology. Axial views were taken in Digital image and communication (DICOM) format with a slice thickness of 5 mm with no gaps between them to construct a 3 dimension (3D) image. A protocol was designed and validated and then applied in volume estimation using MRIcro for image display, Image for volume estimation, and Onis 2.6 as image view. The field of view (FOV) was the area between the xiphosternal notch and iliac crest. Scans were then transformed in DVDs to be analyzed in computer software Image which free download software work in Java script in Microsoft windows. A protocol was designed in which the grid setting was 10. The liver dome was determined at the level of the lower margin of the 8th thoracic vertebra and the lower limit in the scan was determined at the level of the upper margin of the 5th lumbar vertebra (Figs. 1, 2, 3). Measurement was done in the axial view. The protocol was validated by obtaining Cronbach alpha in SPSS version 22. One-way ANOVA was obtained in Microsoft office excels 2007.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All individuals have individual obtained informed consent as well as ethical clearance from the ministry of health, Khartoum, Sudan and from the research committee that belongs to the college of the postgraduate studies, the National Ribat University, Khartoum, Sudan. As seen in Figures 1, 2 and 3.

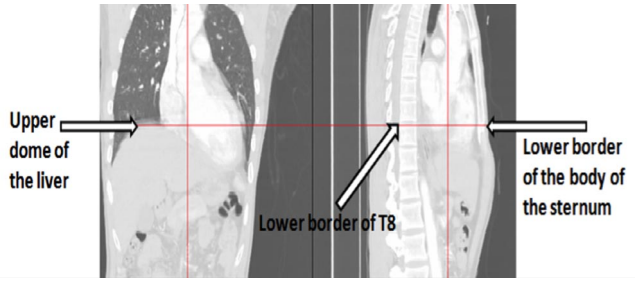

Fig. 1. Determination of the upper margin of liver dome.

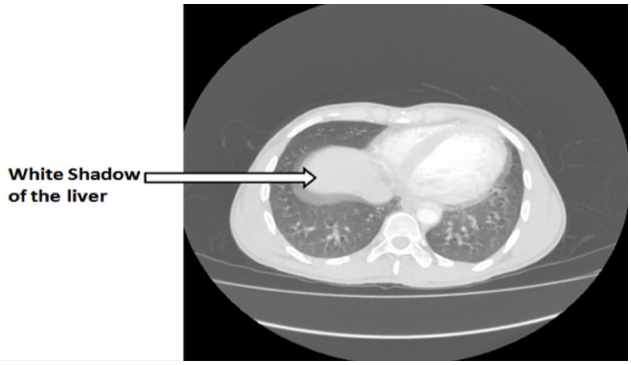

Fig. 2. CT angiography of Toshiba Aquilion™ 64 slice, shows liver dome in an axial CT abdomen.

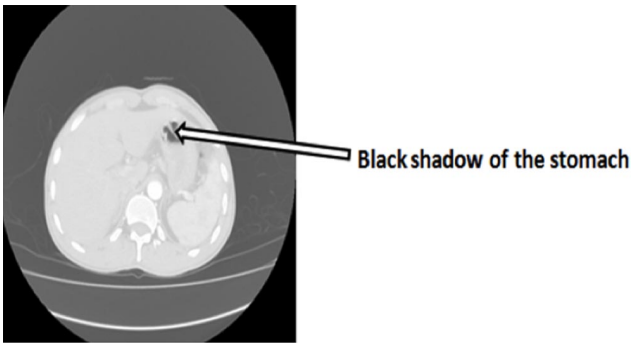

Fig. 3. CT angiography of Toshiba Aquilion™ 64 slice, shows demarcation between liver and stomach in axial CT scan.

RESULTS

The protocol reliability test showed a score of 0.805. The total number of the study population was 300 volunteers. 160 males (53.3 %) and 140 females (46.7 %). 7.7 % (20-29 years, 18.3 % (30-39 years), 18.7 % (40-49 years, 21.3 % (50-59 years), 18 % (60-69 years and 16 % (over 70 years of age). With regards to the relationship of the liver volume with age group, it showed a bell shape curve with a peak at the age group 40 to 49 years regardless of sex specificity. However, the bell shape curve was not typical when each

sex was considered separately (Tables I, II and III). In relation to body mass index, the candidates were tabulated into four groups: underweight 22 %, normal 43.7 %, overweight 21 %, and obese 13.3 % (Fig. 6). Liver volume was found to be significantly associated with body mass index (Table IV).

Table I. distribution of liver volume in cm^3 among the study population according to age groups in years.

Age group	Mean liver volume (cm^3)	Frequency
20-29	3021.94	23
30-39	3241.97	55
40-49	3441.23	56
50-5	3343.15	64
60-69	3289.45	54
>70	3047.53	48

Table II. Mean liver volume in different age groups among males.

Age group	Mean liver volume (cm^3)	P value
20-29	3341.68	0.685
30-39	3248.64	
40-49	3204.00	
50-59	3427.39	
60-69	3280.07	
>70	2951.29	

Table III. Mean liver volume in different age groups among females.

Age group	Mean liver volume (cm^3)	P value
20-29	3288.15	
30-39	2728.84	
40-49	3238.98	0.685
50-59	3678.45	
60-69	3273.35	
>70	3298.82	

Table IV. Mean liver volume in different categories of body mass index.

Body Mass Index	Mean liver volume (cm^3)	P value
Under Weight	2820.27	0.001
Normal	3202.60	
Over Weight	3508.94	
Obese	3791.33	

DISCUSSION

The current study tried to obtain a normative liver volumetry by determining the relationship of the volume with sex, age in years and body mass index among the Sudanese population scanned by CT with contrast compared to literature reports.

The absolute value of the liver volume is reported differently by different researchers. The study of Suzuki *et al*. (2010) was reported an average of 1520 ± 378 cm^3 among the Japanese population. Another study conducted by Fananapazir *et al*. (2015) predicted an average volume of 1753.6 ± 433.3 mL. However, a study by Kamel *et al*. (2001) was compared between two different raters found means of 1807 ± 357 mL and 1788 ± 350 mL. In Germany, Radtke *et al*. (2008) estimated the total liver volume for living donor liver transplantation between 1596 ± 212 mL and 1456 ± 196 mL. In a study among the Chinese population, it was 1205.41 ± 257.53 cm^3 (Feng *et al*., 2017). The current study showed a mean of 3261.32 ± 1365.30 cm^3 which is observed to be larger than the reports in the literature. Liver volume may vary between nationalities since the reports were retrieved from ethnic groups differ in regards to feeding habits and environmental factors. This may shed a light on the possibility of the influence of ethnicity and social habits on liver volume. Regarding the relation to the body mass index, the present study agreed with Um *et al*. (2015) whom reported a significant positive correlation between liver volume and BMI ($p = 0.001$) indicating that patients with a higher BMI may have a larger liver volume. In the current study, the small sample size in each group of BMI may explain the large SD readings in volume. A population-based study is recommended to establish a standard range of volume based on nationality.

When studying the relationship of volume with age, to our knowledge we could not retrieve enough literature. However, some studies showed a significant positive correlation with age (p-value 0.001) (Vauthey *et al*., 2002). The current study showed a steady rise in the volume until the age group of 40 to 49 and then steadily decline in the volume. Yet when compared the volume to age among specific sex it did not show a typical bell shape curve. This may be attributed to the smaller sample size when sex compared separately.

In the analysis of liver volume and sex, liver volume in men is reported to be larger than in women (1831 mL - 1398 mL, respectively) (Andersen *et al*., 2000) following the general role of males larger than females' readings. Interestingly a Korean study showed no significant difference between sexes (641.9 ± 87.7 mL/m^2 in male and 644.4 ± 87.4 mL/m^2 in the female; $p = 0.716$) (Um *et al*.). Interestingly liver volume in this study was smaller in males than in females (3230.64 cm^3 - 3288.15 cm^3, respectively). Estrogens and other hormones related to females may affect fat distribution rendering the tendency of fatty liver among females more than among males. This fact may affect the volume of the liver as an organ surrounded by a considerable amount of fat. Further studies may be needed to validate

the result. Liver volume varies with age and sex and body mass index. Further studies are needed to investigate liver volumetry among different ethnicities and nationalities.

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RESUMEN: La aplicación de la estereología en condiciones hepatobiliares es fundamental en la estimación del volumen hepático. El escaneo topográfico computarizado con contraste es un método confiable en el escaneo del hígado para la demarcación precisa de sus límites. La volumetría hepática varía en función de diferentes factores. Los informes mostraron una correlación del volumen del hígado con el sexo y el índice de masa corporal. No se establece una relación estable entre la edad y la etnia. Este estudio tuvo como objetivo diseñar un protocolo para la medición del volumen hepático de la población sudanesa usando la estereología . El reclutamiento de la población de estudio fue realizado en la clínica de exploración real en Jartum mediante un anuncio de participación. Se excluyeron los pacientes con antecedentes de enfermedades hepatobiliares. Se obtuvo TC de abdomen con contraste en formato DICOM y se transfirió a un software informático para el análisis de imágenes. Se diseñó y validó un protocolo y luego se aplicó en la estimación de volumen utilizando el software MRIcro para la visualización de imágenes, ImageJ para la estimación de volumen y Onis 2.6 como visor de imágenes. Se reclutaron 300 voluntarios sanos. El resultado de la fiabilidad del protocolo fue 0,805. El volumen hepático medio absoluto fue 3261,32 ± 1365,313 cm^3. Se detectó un volumen más elevado de hígado en las mujeres que en los hombres. Se detectó una correlación positiva entre el volumen y el índice de masa corporal (valor de p 0,001) independientemente del sexo. La relación con la edad mostró un aumento continuo y brusco hasta los 50 años, luego comenzó a disminuir de manera constante. Se detectó la relación del volumen hepático con el sexo y el índice de masa corporal. Se necesitan más estudios para investigar la relación entre la etnia y los grupos etarios.

PALABRAS CLAVE: Volumetría hepática; Trasplante de hígado; Tomografía computarizada con contraste; Estereología; Técnica de planimetría.

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