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Human Liver Volume Measurement and Estimation - A Systematic Review

Pam S.D [1]*(FWACS), Dakok K.K[2] (PhD) Sirisena A U.I[1](PhD), Nabasu S.E [2] (MSc)

[1.] Jos University Teaching Hospital Jos, Plateau State, Nigeria.

[2.] Department of Physics, Plateau State University Bokkos, P.O Box 2012, Plateau Sate, Nigeria

Corresponding Author: dakokkyense@gmail.com; **+2348038725719**

ABSTRACT

Several imaging techniques, such as ultrasonography, Magnetic Resonance Imaging (MRI), computed tomography (CT) and Scintigraphy, have been used for the measurement of liver volume (LV). MRI tends to give some advantages over these methods. Measurements performed with sonography may be limited both by the incomplete recognition of the liver contours, due to interference from adjacent intraperitoneal structures and by the technician variability. Scintigraphy may also present a limited capacity to define the liver contours with detail. Several techniques based on manual tracing and semi-automatic and automatic segmentation of liver contours have been successfully applied to CT data to provide liver volume measurements. The stereologic technique has also been combined with CT for the quantification of the size of liver metastases. This research presents a systematic review of some of these imaging techniques in measuring and estimating the human liver volume. Electronic databases such as Ovid, Medline, PubMed, google scholar and z-library were consulted for articles reporting methods of measuring the size of the liver using ultrasound, CT, MRI and other methods. The review concurs with the fact that CT is usually considered as the standard method for measuring liver volume.

Keywords: Liver Volume; Ultrasonography; Magnetic Resonance Imaging, Computed Tomography; Software Assisted Image Post-processing

1.0 Introduction

Measurement of the size of an adult liver anatomy has a great importance in improving the outcome of patients mostly in areas such as planning and follow-up of surgical operations, diagnosis of diseases and monitoring the progression or response of disease treatment over time[1, 2,3 4]. The possibility of post-hepatectomy liver failure in patients undergoing a major hepatic resection is three times higher in patients who are left with less than 25% of their initial liver volume (LV) than those who are left with greater than or equal to 25% of their initial LV [5].The Mortality and morbidity rates for major hepatic resection is known as high as 30% with post-hepatic liver failure being the major cause, hence the knowledge of the pre and post-surgical LV is essential for better monitoring of patients[6]. Hepatic resection is carried out in two separate surgeries in some cases since an increase in LV 6 days after initial surgery makes the second part of the surgery to be successfully carried out with good safety [7].LV knowledge can be used to assessed 3-4 weeks after a portal vein embolization done as part of resection in assessing liver hypertrophy. A 5% increase in LV size is associated with improved patient outcome [8]. Furthermore, LV estimations are mostly used to assess drainage volume before endoscopic biliary drainage [9].Adequate LV reduction is also properly done after a 6-week and 1-week assessment of LV before a gastric banding surgery [10].

Measurement of LV over the years have been carried out using different methods. Computed Tomography (CT) is presently seen to be the gold standard for assessing the volume of the adult liver[11] and it has been used to assess graft sizes for living-related liver transplantation [12, 13, 14, 15]. Magnetic Resonance Imaging (MRI) has also proven to be an another accurate means in which LV is measured [16]. In spite of the advantage that MRI offers in not using ionizing radiation, CT is seen to be more preferred to it because it is readily available, faster and less expensive to perform. Before the advent of automated methods of CT liver measurement, measurement of LV from CT images was performed manually, a method done by manually tracing the liver boundary on each CT slice to measure the volume of liver on each slice. The volume of individual slicewas then added up to get the total volume of the liver. A more latest improvement in CT imaging technology is the introduction of software programs that automatically calculate liver volume [17]. This method is less operator dependent. The method has been developed more into a multiple automated and semi-automated liver segmentation tools and are commonly referred to as software assisted image post-processing (SAIP) tools[17]. SAIP tools have gained more popularity and acceptance, thus proving to be very accurate in predicting liver volumes [18, 19]. Recent studies on the use of SAIP revealed that measurement of LV correlate well with manual method [20], and with the added advantage of being a substantially faster method of volume estimation [21].

The liver is a major organ that is found only in vertebrates performing a lot of essential biological functions such as detoxification of the organism, and the synthesis of proteins and bio-chemicals necessary for digestion and growth [22, 23]. In humans, it is located in the right upper quadrant of the abdomen, below the diaphragm.It is a reddish-brown, wedge-shaped organ with two lobes of unequal size and shape. A human liver normally weighs approximately 1.5 kg [24] while its maximum cranio-caudal dimension (CC) and antero-posterior dimension (AP) are 15cm and 13cm respectively, with maximum for both dimensions together as 28cm [25, 26, 27].The average volume of the liver estimated using water displacement method is 1434±503ml. In all cases, the liver weight (in grams) exceeds the amount of liver volume (in milliliters). The average density of liver tissue is1.14±0.16g/ml [28].

The calculations of the LV using an equation to convert simple sonographic measurements into a volume represent a group of volumetric methods. Volumetric techniques are quick and easy procedures for measuring the liver. In most volumetric methods, the product of three mutually perpendicular dimensions of the organ are used. The calculating equation consist in product of simple liver measurements and the coefficients based on regression analysis. These methods were not widely used in clinical ultrasound due to the technical complexity to measure the accurate transverse dimension of the liver and the lack of generally accepted standards of the liver volume. The difference in actual liver volume (ALV) and standard liver volume (SLV) is considered more sensitive than total liver volume (TLV) alone because of the large variability in liver size based on race, sex, body shape and body size [29,30,31,32]. Furthermore, the SLV formulas derived from various ethnic groups may not be comparable with each other. Indeed, discrepancies have been observed between formulas for various Asian populations [31,32]. Thus, at present there are no formulas for assessing SLV that are generally accepted in Chinese or Western centers [31,32]. However, as for TLV, differences in race, sex, body shape and size, and measurement method can also affect these indices.This manuscript gives a review of information on the different ways by which the human LV is measured and estimated using ultrasound, MRI, CT and other methods.

1.1 Search Method

Electronic databases such as Ovid, Medline, PubMed, google scholar and z-library were consulted for articles reporting methods of measuring the size of the liver using ultrasound, CT, MRI and other methods. Search terms used for each database were ultrasound, sonography, ultrasonic, ultrasonography, CT of the liver, MRI of the liver, sonographic measurement, hepatomegaly, liver enlargement, liver size, and liver measurement.

2.0 Measurement of Liver Volume methodologies

2.1 Measurement from Anthropometric Variables

LV can be estimated from measured anthropometric values such as body weight (BW), body height (BH), liver weight (LW), body surface area (BSA), body length (BL) and age. A Japanese study enables the calculation of total liver volume (TLV) from BSA. This formula has been applied to calculate the graft to TLV ratio for living related donor liver transplantation [33, 34] and the future liver remnant (FLR) to TLV ratio before liver resection [35]. Table 1 gives a summary of different estimation formulae involving these anthropometric variables and their estimated LV.

Table 1: Formulae for Estimating Human Liver Volumes Using Anthropometric Measurements

Authors	LV formula	LV (ml)
[36]	$LV = 21.585 \times (BW)^{0.732}Kg \times (BH)^{0.225}cm$	1663.8 ± 366.1
[37]	$LV = 5\ 1072.8 \times BSA(m^2) - 2\ 345.7$	322.6 ± 335.8
[38]	males: $SLV = 691.90 \times (BSA)^{1.06}$; females: $SLV = 663.19 \times (BSA)^{1.04}$	1180.5 ± 137.4
[39]	$LV = 706.2 \times BSA\ (m^2) + 2.4$; $LV = 2.223 \times BW\ (kg)^{0.426} \times$ body height (BH) $(cm)^{0.682}$	1149 ± 142
[40]	TLV = 203.3 - 3.61 × age + 58.7 × thoracic width - 463.7 × race (Asian = 1, Caucasian = 0); TLV = 2670.1 - 1.95 × age + 70.8 × sex - 1940.5 × BSA + 761.2 × BSA2 - 420.1 × race race (Asian = 1, Caucasian = 0); TLV = 1222.1 - 3.24 × age + 210.7 × sex + 18.8 × BMI - 505.8 × race race (Asian = 1, Caucasian = 0)	1092 ± 425 for Asian 1622 ± 735 for Caucasian
[41]	$TLV = -794.41 + 1,267.28 \times BSA\ (m^2)$; TLV = 191.80 + 18.51 × BW (kg)	1,518 ± 244
[42]	SLV = 908.204 × (BSA) – 464.728 for DuBois body surface area (BSA) SLV = 893.485 × (BSA) – 439.169 for Monsteller BSA	1117.5± 324.2 745.4 ± 155.1
[43]	LV = 1000 (0.72√BSA+0.171)3	1438.45±182.87
[44]	LV = 452+16.434(BW)+11.85(age) –166(sex factor); Female factor = 1, Male factor = 0	1841.51±212.13
[45]	SLV = –456.3+969.8×BSA	1549.63±189.51
[46]	SLV = 706.2 × (BSA) + 2.4	1221.0±141.0
[47]	SLV = 772 × (BSA)	1329.0±154.0
[48]	SLV = 1267.28 × (BSA) − 794.41	1392.0± 253.0

Most of these formulae in table 1 showed overestimated or underestimated values of LV and SLV even though standard liver SLV measured based on patient characteristics such as body surface area (BSA) and body weight, is a good reflection of the hepatic metabolic demands of the individual patient [15]. Possible reason for these overestimations is due to other structures attached to the liver (the gallbladder, ligaments, and vessels) and perimortem cardiovascular events (hypovolemia and heart failure) that could have resulted in fluid shifts and heavier liver weights [49]. However, some results of SLV estimation in table 1 were not significantly different (p = 0.0001) from the mean actual value [46, 47, 48].Therefore, with these irregularities in the values of LV and SLV, there is need of a new formula to estimate liver volume using anthropometric measurements to be more consistent with actual values.

2.2 Ultrasonography method

Liver volume can be measured by the water displacement method or calculated indirectly by liver weight[36], but these methods are only restricted to autopsy or intra-operative use. Several other methods have been employed for noninvasively measuring the liver volume using imaging such as ultrasonography[30].Ultrasound is an imaging technique that uses high-frequency sound waves not audible to the human ear to create a 2D gray-scale image of structures within the body [50]. Diagnostic ultrasound was developed in the 1940s and has since turned into a generally acceptable method of the medical imaging [51]. Ultrasound allows rapid assessment of the liver and its related vasculature. The normal sonographic appearance of the liver is that of a homogeneous light gray structure containing dark vessels and bright ligaments. Recent advances in ultrasound have seen the liver able to be scanned using a 3D ultrasound technique. This technique requires more expensive, less portable equipment and greater training time, which limits its accessibility to many departments and clinicians.

One of the earliest methods of LV estimation using ultrasound was carried out with the aid of 3.5 MHz linear array probe (Aloka SSD-280) [36]. The patients weremade to lie down in a dorsal position, and held their breath at the end of inspiration. Theircranio-caudal (CC) and the antero-posterior (AP) diameters were determined on a longitudinal scan, along the mid-clavicular line, and parallel to the xypho-umbilical line. The probe was kept perpendicular to the body surface. The maximum latero-lateral (LL) diameter was measured in a transverse subcostal scan. The probe was kept perpendicular to the xypho-umbilical line, and rotated upwards to obtain the maximum diameter. The LV for the patients were then estimated using the equation 1(R^2=0.756)

$$LV = 133.2 + [0.422 \times (CC) \times (AP) \times (LL)] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 1$$

The average LV gotten from the above equation for a number of 22 patients was 1248 ml, which is about 12% less than the standard value obtained by water displacement method [28]. This shows that this method of LV estimation is good and accepted.Another Ultrasound method was carried out on 55 patients which resulted in an average LV of 1636 ml using the equation 2 [52]

$$LV = 343.71 + (0.84 \times CC \times AP \times LL) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 2$$

This equation is too inaccurate to be of clinical use for estimating LV even though it holds potential to be of use in tracking disease progress or response to treatment over time in individuals, and is certainly substantially better as an indicator of overall liver size than the linear measurements.

2.3 Magnetic Resonance Imaging method (MRI)

MRI is considered to be a powerful tool for the detection and characterizing the liver pathology [53]. It can provide accurate LV measurements, as shown by comparisonof magnetic resonance organ volume measurements in cadavers, animals, and patients with the actual LV determined by water displacement [54, 16]. Most of the studies dealing with Magnetic resonance LV have used the planimetrictechnique, which relies on the precise manual tracing of liver boundaries in all sections crossing the liver[16, 55, 56, 57,58, 59]. Two studies have reported liver volume measurements based on three-dimensional (3D) magnetic resonance imagesof the liver [60, 61]. However, the 3D reconstruction alsorequires the manual or semi-automatic segmentation ofhepatic boundaries in all 2D magnetic resonance images through theliver. Simple linear measurements have also been applied to magnetic resonance images in order to generate the liver volume index[62].

MRI of the liver was introduced to perform tumor screening, assess vascular patency, and estimate liver sue in order to decrease the number of tests and avoid potentially nephrotoxic iodinated contrast agents [16]. The LV was calculated from the averaged transverse and coronal planes. Calculation of the volume was performed using the standard software of the scanner where the outline of the liver in each individual image was traced with a cursor, after which the area was calculated. The volume of the liver was then computed (in milliliters) for each orientation by adding all area measurements for that orientation. The results show that liver volume calculated from transverse and coronal MRI(1986$\pm$568 ml) accurately predicts the displacement volume of the explanted liver (1884$\pm$631). The displacement volume also correlated closely to explant mass. By this result, MRI offers an anatomically accurate means of determining the adult liver volume in vivo. In addition to its ability to assess vascular patency and screen for tumors, MRI can accurately predict liver volume to match potential donor organs and help gauge prognosis.

MRI and stereology can be used to estimate liver volume and compare the liver volume estimations with the real liver volume measurements [63]. A reliable formula was provided for estimation of the coefficient of error, which allow the calculation of the optimum number of sections required to attain a given precision for a particular scanning direction. The formula was based on the Cavalieri principle of volume measurement by means of consecutive serial sections written as equation 3 [63].

$$V = t \times a/p \times (P_1 + P_2 + \cdots + P_n - P_{max}) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 3$$

where $(P_1 + P_2 + \cdots + P_n)$denote the point counts, P_{max} is the maximal number of points counted on a single scan plane of the subject and (a/p) represents the area associated with each test point, corrected for any change of scale in the images as it is printed on the hardcopy films.The volumes of five livers estimated by means of Cavalieri principle changed between 857 and 1592 ml . The mean of liver volume determined by the Cavalieri estimator and water displacement technique was highly correlated (r = 0.993). This method of estimation of volume is notably independent of both shapes and orientation of the object, inexpensive and fast, since point counting is carried out within 5-10 min per subject.LV was also estimated using the techniques of planimetry andpoint counting, in combination with the Cavalieri method of modern design stereology [64]. A systematic slice sampling procedure was performed to estimate liver volumes using both volumetric techniques. The point counting technique was optimized by altering the point spacing of the grid. The agreement between the two techniques was found. Measurement repeatability of both volumetric techniques was also evaluated. The estimated average LV for point counting and planimetry methods were found to be 1477.7 ± 230.7 ml and 1480.1 ± 229.6 ml respectively, whose difference was considered statistically significant ($P<0.05$).The point counting technique was found to be considerably faster than planimetry, simple and easy to handle, in comparison with planimetry. Therefore, it may be considered a more efficient approach in estimating liver volume from MRI than the conventional technique of planimetry.

2.4 Computed Tomography (CT) Method

Computerized tomography (CT) visualizes the liver as a series of sequential, contiguous cross-sectional images, each image representing a slice of tissue of a specified thickness. Typically, 10 images are needed to examine the entire liver. The volume of the liver can be calculated by obtaining the area of each cross-sectional image, multiplying the area by the slice thickness to give slice volume, and finally summing the volumes of slices to give liver volume as shown in the formula below [65]

$$LV = \sum_i^n (A_i d_i) \qquad \text{……} \; 4$$

Where A is the slice sectional area written as;

$$A = \frac{28.4}{Standard\ tracing\ weight} \times tracing\ weight$$

and d is the slice width. This ancient method though effective, but laborious and conducted without organ motion and the borders of most organs were clearly defined. Computerized tomographic scanners now, however, are being equipped with software programs that allow the user to select an irregular region of interest, the actual area of which is calculated and displayed on the CT.

A good example of this new method of LV measurement was carried out using a CT-Volume Software (Siemens Syngo Multimodality Workplace; Version VE52A) [66]. An interactive volumetry was performed and traced the liver contour on each CT slice very carefully. The number of slices in each case had an average of 7, and all remaining slices were stained by the program automatically. Volume was determined by multiplying the sum of all slices by the 3D image reconstruction and volume-rendering tool which took 25–30 minutes per case. The average LV measurement was found to be 1315.24 ± 338.75 ml showing that the method of LV estimation is very accurate.A similar experiment was conducted where Estimation of LV using CT was measured using Able 3D Doctor 3.5 (software) in axial CT image [67]. The LV was measured through contiguous slices. The software enabled free hand outlining of the perimetry of liver by digital pen. Volume was determined by multiplying the sum of all slices by the 3D image reconstruction and volume-rendering tool resulting to an average LV of 1572.5±550.5 ml.

A study was put forward to investigate the intra and inter- rater reliability of a specific SAIP tool, namely, the Philips liver segmentation and analysis package (Eindhoven, The Netherlands) [68]. The reliability testing of this tool was undertaken as a preliminary investigation to establish the reliability of two observers who were to take part in a larger study. This Philips liver segmentation and analysis package (Eindhoven, The Netherlands) provides an automatic volume calculation of the liver by highlighting the liver tissue within each slice and then summing the individual slice volumes. The mean LV obtained in this research was 1615.9±390.0. The advantage of SAIP tools is in their ability to quickly and accurately calculate liver volume automatically with only fine adjustment required by the operator. This study concludes that liver volume measurements of both normal and abnormal livers using the Philips SAIP (Endhoven, The Netherlands) is considered very reliably, with confidence that different CT operators can get the same results. SAIP has been proven to be the most accurate method for calculating LV which reports calculated versus actual volume difference of approximately 17.5 ml and a percentage of error of approximately 2.8 % [69, 70].

3.0 Conclusion

Major imaging techniques including ultrasonography, MRI computed CT and anthropometric methods for measurement of liver volume have been systematically reviewed in this paper. Among all these methods, CT is usually considered as the standard method for measuring liver volume.This review provides relevant information for researches who may want to get precise information on the methods of LV measurement and estimation, however, it does not give detailed description of the procedures by which these methods are operated. With different formulas and approaches to measuring the human LV, results show that reliable measurements are possible.

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