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The development of a practical and uncomplicated predictive equation to determine liver volume from simple linear ultrasound measurements of the liver

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ABSTRACT

This study sought to develop a practical and uncomplicated predictive equation that could accurately calculate liver volumes, using multiple simple linear ultrasound measurements combined with measurements of body size. Penalized (lasso) regression was used to develop a new model and compare it to the ultrasonic linear measurements currently used clinically. A Bland–Altman analysis showed that the large limits of agreement of the new model render it too inaccurate to be of clinical use for estimating liver volume *per* se, but it holds value 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 ultrasonic linear measurements currently being used clinically.

Ultrasound evaluation of the size of the liver can be useful for clinicians to aid in the diagnosis of liver disease or to track disease progress and response to treatment/intervention over time.[1,2] Ultrasound is a readily available, inexpensive and comparably fast imaging technology which does not use ionising radiation. Liver size is usually determined using single linear measurements rather than an estimation of liver volume. Volume calculations of the liver are more easily and rapidly undertaken from Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scans and are regarded as gold standard.[3] These imaging modalities are expensive compared to ultrasound, are far less mobile and accessible and have the additional disadvantage of radiation exposure associated with CT[4] and claustrophobia associated with MRI.[5] Liver size can also be assessed through clinical examination using a palpation/percussion technique, however multiple studies have shown this technique to be innacurate.[6–8]

In the current Australian clinical environment the liver is commonly measured during a routine upper abdominal ultrasound. Measurement of liver size using ultrasound is most often determined by taking a simple linear measurement of the liver from a plane along the mid-clavicular line, and using cut off values to differentiate normal from abnormal liver size. Within the literature, two methods have been described using this plane: measuring the maximum width between the anterior and posterior borders of the liver and measuring the distance between the liver dome to liver tip, with both methods using different upper limits to differentiate normal from enlarged livers.

Niderau et al. (1983)[9] used the method measuring the maximum width between the anterior and posterior borders of the liver in 915 participants with normal livers to determine normal liver size. They determined an upper limit cut off value of 11.3 cm for normal livers. Reliability and accuracy of this technique was not reported and the upper limit cut off value was not tested for its effectiveness in detecting enlarged livers.

Two studies used the liver dome to liver tip method.[10,11] Kratzer et al. (2003)[11] determined 16 cm to be the upper limit cut off value for normal livers from a sample of 2080 normal participants. Accuracy and rater reliability for the measurement method was not reported. Gosink & Leymaster (2005)[10] determined 15.5 cm as the

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cut off measurement for normal using the same measurement technique, but used a sample of 36 cadavers whose ultrasound images were retrospectively assessed. They demonstrated that this technique and cut off value was accurate in determining enlarged livers in 75% of cases. The position of the mid-clavicular line was determined by individual judgement from the images only and accuracy and reliability for the method was not reported.

While the single, simple linear ultrasound measurements of the liver described above are easy to perform, they are limited in that they provide dimensional information at only one site within one lobe (Rt) of the liver. Calculation of liver volume gives a more complete picture of liver size compared to single linear measurements. Calculations of liver volume using ultrasound have been described, but the methods are time consuming involving performing area calculations of multiple ultrasound images, and many of the reported methods use equipment that is now out of date.[12] The prediction of liver volume using multiple simple linear ultrasound measurements of the liver would be practical and rapid. There have been some attempts to predict liver volume from simple linear ultrasound measurements of the liver, three studies could be found in the literature Elstein et al. (1997),[1] Glenn et al. (1994),[13] Zoli et al. (1989),[14] that have previously developed equations to determine liver volume from simple ultrasound measurements of the liver. The equations developed by these other studies all used the variable of maximum anterior to posterior diameter (MaxAP) *maximum longitudinal diameter (MaxLong)*maximum transverse diameter of the liver(MaxTrans). However, we have previously demonstrated that the above three measurements are not as reliable as those used in this study,[15] and further, each of the above papers suffered from either very small sample sizes, equipment now obsolete, or a comparatively simplistic statistical analysis.[12]

This study aimed to use multiple simple linear ultrasound measurements combined with measurements of body size to develop a practical and uncomplicated predictive equation that could accurately calculate liver volumes equivalent to liver volumes determined from CT scans.

Methods

Ethics approval was sought and granted from the ethics committee of the University of South Australia to recruit patients from a private radiology provider who were referred to the practice by their medical practitioner to have an upper abdominal CT scan which imaged their entire liver as part of their medical care. The patients were referred for multiple reasons, not necessarily liver related.

A consecutive sample of 55 consenting participants was recruited (23 male, 32 female, mean age (SD) 62.3 (15.7) years. An information sheet was provided to participants and written consent was obtained prior to their CT scan. The participants were informed that they could withdraw from the study at any time without prejudice.

Body measurements

The height, weight, age, sex and waist circumference of each participant was collected. Body Mass Index (BMI) was calculated from height and weight. Waist circumference was measured at the point midway between the lower margin of the rib cage and the anterior superior iliac spine from the CT images using a trace measurement tool.

CT liver volume measurements

CT examinations were undertaken by one of two qualified CT technicians on a Philips Ingenuity 128 slice low dose machine with i-dose 4 software (Philips Medical Systems, Best, Netherlands). The participant was positioned supine on the CT table in a state of respiratory inspiration during image collection. A standardised abdominal imaging protocol with contrast media was used.

Liver volume ($Volume_{CT}$) of each participant was calculated from the stored CT images by one of two qualified CT technicians. Volume was initially calculated automatically from the thin slice data using the inbuilt liver segmentation and analysis software (Philips Healthcare, Eindhoven, The Netherlands). Guided by vascular landmarks and liver segments, the liver segmentation and analysis software identifies and highlights liver tissue in the data set. The CT technicians then accessed individual slices and manually made adjustments to remove tissue incorrectly included in the measurement or add tissue incorrectly excluded. The reliability of this technique has been demonstrated in a previous study which showed two qualified CT technicians could achieve high intra- and inter-rater reliability.[16] Fig. 1 shows an example of a reconstructed liver and volume calculation performed by this software.

Simple linear ultrasound measurements

Within 10 min of the CT examination each participant underwent a targeted ultrasound scan where two static images of the liver were taken and stored to the ultrasound machine. A full liver ultrasound assessment was not conducted. Ultrasound images were taken by one of two qualified sonographers on a Philips IU22 Ultrasound System (Philips Healthcare, Bothell, WA) set to an abdominal imaging protocol with a C9-4 curved array transducer. Scanning parameters (depth, gain and TGC) were optimised for each participant. Each participant was positioned supine on the ultrasound bed with their body tilted 45° to the left away from the examiner. The participant's skin was exposed from their xiphisternum to their waist, and images taken in a state of inspiration. The first image was taken with the transducer orientated longitudinally in a plane that was in line with the midpoint of the participant's clavicle (or the mid clavicular line). This image (Image A/B) is representative of the right lobe of the liver (Fig. 2). The second image was taken with the transducer orientated longitudinally along the midline at a point in line with the participant's xiphisternum. This image (Image C) is representative of the left lobe of the liver (Fig. 2).

The ultrasound images were accessed at a date within a period three months after image collection. One sonographer accessed the images to make three simple linear measurements of liver size using the machine's inbuilt callipers. The diameter of the right lobe of the liver from dome to tip (Rt lobe DT) and the maximum anterior to posterior diameter of the right lobe of the liver (Rt lobe AP) was made from Image A. The maximum anterior to posterior diameter of the left lobe of the liver (Lt lobe AP) was made from Image C (Fig. 2). These simple linear ultrasound measurement planes can also be seen in Fig. 2.

Reliability of the simple linear ultrasound measurements

The simple linear ultrasound measurements performed were selected from a previous study[15] in which they were demonstrated to have high intra-rater and inter-rater reliability (intra-rater ICC values of 0.963 for Rt Lobe DT, 0.974 for Rt Lobe AP, and 0.909 for Lt Lobe AP and Inter-rater ICC values of 0.930 for Rt lobe DT, 0.834 for Rt lobe AP and 0.865 for Lt Lobe AP).