Current possibilities of liver volume estimation in diagnostic ultrasound (ex vivo study)

Abstract

Ultrasound evaluation of the liver volume can be useful for clinicians to aid in objective quantitative assessment of the liver size. For some organs (for example thyroid gland, testicles, ovaries) in diagnostic radiology the volume is the most objective criterion for estimation its size. Today CT and MRI imaging modalities use an objective techniques for volume calculation of the liver. MRI and CT-based liver volumetry are regarded as gold standard for evaluation of the liver volume.¹⁻⁴ Nevertheless currently the ultrasonic linear measurements being used clinically as an indicator of overall liver size. Up to date in clinical sonography the ultrasound report contains only the linear measurements of the liver.⁵ Surely this fact significantly reduces the diagnostic value of the clinical estimation of the liver size.

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Introduction

At present, the linear measurements of the liver are included in the actual diagnostic ultrasound scan protocol. 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 measurements of the liver from a plane along the mid-clavicular line, and using cut off values to differentiate normal from abnormal liver size.⁶ One measurement of liver size is done in the mid-clavicular line from highest peak of the right hemidiaphragm down to the caudal liver end (maximal cranio-caudal diameter-Max CC). This has a maximum dimension 18cm. Another possibility to measure the liver size is in the mid-clavicular line to measure cranio-caudal dimension (CC) and antero-posterior dimension (AP). The maximum CC is 15cm and AP 13cm, maximum for both dimensions together is 28cm.^{5,7,8}

An attempts to estimate the liver volume on the basis of sonographic liver measurements have a long history.⁹⁻¹¹ The complexity of calculating the liver volume is due to irregular geometric shape of the liver, which cannot be approximated to an ellipse. In systematic review of J. Childs et al.¹² the methods of assessment of the liver size using 2D ultrasound are divided into 4 groups: volume measurements, body ratio measurements, representative measurements, and volumetric measurements. A volume measurement is a layer-by-layer measurement technique that resulted in an estimate of the overall volume of the liver. Body ratio measurements are those that measured the size of the liver as a ratio to body size. Representative measurements are those that do not reflect the true volume or size of the liver in more than one dimension. Volumetric measurements are those that use simple measurement techniques to develop a hepatic volumetric index (HVI) and then use a mathematical formula to translate this into a true liver volume.¹²

The calculations of the liver volume using an equations to convert simple sonographic measurements into a volume represent a group of volumetric methods. Volumetric techniques promise to be a quick and easy way to measure 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. In recent years, a new calculation formula of the liver volume was proposed.^{13,14} New formula does not require the transverse measurements of the liver. It is advantageous in that they are simple and rapid to perform, and can be reproduced easily on modern-day equipment. That is why it could be include into routine ultrasound examination.

The ability to convert simple liver measurements into a volume using an equation would be of great value in a clinical setting. Using multiple simple measurements to generate a liver volume would be superior to that of using only a single or several measurements, which gives a semiquantitative estimate of liver size.¹³

The aim of the study

Ex-vivo to assess the liver volume calculation volumetric formulae

Tasks

- To estimate the liver weight after extraction from the cadaver abdominal cavity.
- To estimate the liver volume using water displacement method.
- To calculate the liver volume using clinical ultrasound volumetric formulae
- To compare the results of the liver volume calculation with real liver volume and to select the optimal liver volumetric formula.

Material and methods

The study was performed on 34 cadavers of persons who died as a result of various diseases studied in the Bureau of forensic medical examination of the Kaliningrad region. All the forensic examination

were performed in accordance with the Order of the health Ministry of the Russian Federation from may 12, 2010 # 346-n “On approval of the procedure for the organization and production of forensic medical examinations at state forensic expert institutions of the Russian Federation”. The corpses were studied by the method of Shor. Among the investigated corpses were 20 men and 14 women aged from 28 to 96 years. The cause of death are shown in Table 1.

Table 1 The cause of death and the number of observations (n)

The cause of death	N
Pancreatic cancer	1
Obstructive asphyxia	1
Hemorrhagic stroke	1
Hanging	1
Burn disease at the stage of septicotemia	1
Pulmonary embolism	1
Hypothermia	1
Empyema	1
Urinary bladder cancer	1
Bilateral subtotal pleuropneumonia	1
Poisoning by unknown substance	1
Ischemic cardiomyopathy	1
Cirrhosis of the liver.	2
Acute myocardial infarction	2
Alcohol cardiomyopathy	3
Atherosclerotic heart disease	15

During the forensic autopsy the liver was extracted from the abdominal cavity. After the removal of the gallbladder and ligaments the liver were weighed and then placed in a container of water to determine body volume by measuring the volume of displaced fluid.

Measurement of the liver size was performed on the liver specimens according to the rules to require liver diameters in clinical ultrasound.⁷ For this purpose we carried out two sections of the liver specimen in parasagittal plane. Right lobe was dissected at the level of the highest point of the diaphragmatic surface (Figure 1). The left lobe was dissected close to the falciform ligament (Figure 2).

Figure 1 Schematic representation of the liver right lobe section to measure the cranio-caudal size of the right lobe (CCRL, A), antero-posterior diameter of the right lobe (APRL, B), and maximal cranio-caudal diameter of the right lobe (maxCCRL).

Figure 2 Schematic representation of the liver left lobe section to measure the cranio-caudal size of the left lobe (CCLL, A) and antero-posterior diameter of the left lobe (APLL, B).

Liver width was measured at the outermost lateral points of the two lobes in horizontal plane (Figure 3). Microsoft Excel software was used for analyzing the data. For continuous variables, mean, maximal, minimal values and standard deviation was used. The volume difference between the calculated liver volume (CLV) on the base of each liver volumetric formula and actual liver volume (ALV) estimated using water displacement method was demonstrated with the percentage error $[(CLV-ALV)/ALV \times 100]$.

Figure 3 The width measurement of the liver.

Results

The average weight of liver according to results of post-mortem weighing was 1607±562g. The average volume of the liver estimated using water displacement method, was 1434±503ml. In all cases, the liver weight (in grams) exceeds the amount of liver volume (in milliliters). The average density of liver tissue was 1.14±0.16g/ml.

Mean values of liver volume were calculated using five formulas.^{13,15-19}

The average liver volume calculated using formula of JT Childs et al.,¹⁴ was 1355±487 (range 668-2631)ml. The results of the measurements and calculated liver volume are presented in Table 2.

Table 2 The post-mortem weight of the liver and the LVC using different available formulae. The percentage of deviation of calculated liver volume in comparison with the actual volume of the liver estimated using water displacement method

№ of study	Liver weight (g)	The actual liver volume (displacement, ml)	Liver volume calculated using various volumetric formulae. (ml)						The percentage of deviation of calculated liver volume in comparison with the actual volume of the liver estimated using water displacement method			
			Glenn D ¹⁷	Zoli M ¹⁵	Patlas ¹⁶	Elstein ¹⁸	Childs JT ¹³	Glenn D ¹⁷	Zoli M ¹⁵	Patlas ¹⁶	Elstein ¹⁸	Childs JT ¹³
1	2121	1840	2640	2941	2867	2455	1547	43	60	56	33	-16
2	1015	620	1222	1448	1343	1309	990	97	134	117	111	60
3	2593	2000	2303	2611	2531	2182	1183	15	31	27	9	-41
4	798	672	934	1104	991	1076	863	39	64	47	60	28
5	1801	1697	1675	1369	1262	1675	1285	-1	-19	-26	-1	-24
6	1400	1180	1561	1306	1198	1583	1136	32	11	2	34	-4
7	1279	1100	2316	1596	1494	2193	1505	111	45	36	99	37
8	1736	1650	2620	2129	2038	2438	1637	59	29	24	48	-1
9	1152	950	1620	1364	1257	1631	1225	71	44	32	72	29
10	2143	1800	3209	2477	2393	2915	2018	78	38	33	62	12
11	1669	1425	3129	2004	1910	2850	1700	120	41	34	100	19
12	826	690	895	841	722	1044	687	30	22	5	51	0
13	2300	2080	3017	2631	2551	2760	2136	45	26	23	33	3
14	1134	980	1675	1170	1059	1674	1177	71	19	8	71	20
15	2711	2475	4669	3288	3222	4095	2631	89	33	30	65	6
16	1982	1935	2591	1894	1798	2415	1133	34	-2	-7	25	-41
17	2103	1980	3371	2217	2128	3046	1785	70	12	7	54	-10
18	1765	1460	2882	1712	1612	2651	1689	97	17	10	82	16
19	1657	1577	1643	2106	2015	1649	1079	4	34	28	5	-32
20	1335	1210	1452	1085	972	1495	976	20	-10	-20	24	-19
21	909	695	1224	1107	994	1310	1063	76	59	43	88	53
22	1725	1490	2352	1990	1896	2222	1521	58	34	27	49	2
23	1271	1172	1669	1378	1271	1670	887	42	18	8	42	-24
24	1167	1011	1245	1032	918	1327	1071	23	2	-9	31	6
25	1236	1070	2227	1484	1379	2121	977	108	39	29	98	-9
26	2047	1660	2741	2213	2124	2537	1666	65	33	28	53	0
27	943	800	1097	1200	1089	1208	850	37	50	36	51	6
28	2110	1923	3164	2897	2823	2878	2403	65	51	47	50	25
29	913	824	1305	1076	962	1376	711	58	31	17	67	-14
30	744	1562	1229	1000	885	1315	668	-21	-36	-43	-16	-57
31	1562	1430	2879	2534	2452	2648	1312	101	77	71	85	-8
32	1779	1530	2013	1743	1644	1948	1026	32	14	7	27	-33

Table Continued...

Liver volume calculated using various volumetric formulae. (ml)								The percentage of deviation of calculated liver volume in comparison with the actual volume of the liver estimated using water displacement method				
33	2015	1977	3854	2702	2623	3436	1883	95	37	33	74	-5
34	2706	2300	4369	3286	3220	3853	1640	90	43	40	68	-29
M	1607	1434	2259	1851	1754	2147	1355	56	32	23	53	1
CO	562	503	979	709	725	791	487	35	31	30	31	27
Min	744	620	895	841	722	1044	668	-21	-36	-43	-16	-57
Max	2711	2475	4669	3288	3222	4095	2631	120	134	117	111	60

(M, arithmetic mean; SD, standard deviation; Min, Max, minimum and maximum value).

We have determined the percentage deviation of liver volume calculated based on volumetric formulae with respect to the actual volume of the liver estimated using water displacement method. It was discovered that the average percentage deviation of the calculated liver volume varies widely up to 56% formula¹⁷ compared to the AVL. The lowest percentage average deviation (1%) were found in the formula Childs JT.¹⁴ At the same time, the standard deviation of errors of calculation of the liver volume according to the formula is approximately the same (27%) JT Childs,¹⁴ up to 35% Glenn D.¹⁷

Discussion

The liver volume and the liver weight

In our study the liver weight (in grams) exceeds the amount of liver volume (in milliliters). Post-mortem extracted from the cadaveric corp liver specimen sinks when water displacement method occurs. In our study it is shown that the weight and volume of the liver are not identical variables. The average value of the density of liver tissue determined as 1.14g/ml, a standard deviation -0.16g/ml.

The issue of the density of the liver tissue has already been discussed the scientific literature. It was initiated by the fact that preoperative determination of the liver mass volume using CT-volumetry exceeds the actual volume of the resected mass, measured using water displacement method.²⁰ SM Niehues et al.²¹ carried out a pilot study aimed at a systematically determine the difference between the results of *in vivo* CT liver volumetry and *ex vivo* water displacement liver volumetry in a pig animal model. The authors showed that the median density of liver tissue is 1.07g/ml. Regression analysis showed a high correlation ($r^2=0.985$) between the results of CT volumetry and the water displacement method. CT volumetry was found to be 13% higher than the water displacement volumetry ($p<0.0001$). The reason of difference between *in vivo* CT-volumetry and *ex vivo* water displacement volumetry seems to be blood perfusion of the liver.

K. Kitajima et al.²² analyzed the volume of the liver specimen calculated by the water-displacement method and the volume liver fragment determined preoperatively by ultrasonography. As the volume of each compartment assessed by ultrasonography included blood volume and there was no blood in the large vessels of the resected specimens they assumed that the ultrasonography-visible vascular bed represented 15% of the whole liver volume and, thus, added 15% increment to the specimen volume before comparison. The percentage difference between the ultrasonography volume and specimen volume (plus 15% increment) was calculated according

the equation: (ultrasonography volume – specimen volume*1,15)/specimen volume *100).

It is known that in the norm 100g of liver tissue contains 25-30ml of blood.^{23,24} However, the exact distribution of blood volume between the large and small intrahepatic vessels is still not known, as it is not known what amount of blood is visualized in the intrahepatic vessels at sonography, and accordingly, the extent to which this affects the volume of the organ. Normally, 100 g of liver contains 25-30ml of blood.^{23,24} However the respective distribution of blood volume between the intrahepatic large and small vessels is not clear, no is amount of blood in the intrahepatic vascular bed, vizulised by echography.²²

In our study, the mean density of liver tissue was 1.14 ± 0.16 g/ml, which exceeds the same results of Niehues SM et al.²¹ Surely, the liver of pigs and humans may have different density of the tissue. However, O Garkavenko et al.²⁵ it was shown that healthy liver tissue has a density in the range of 1.02 to 1.09g/ml, which corresponds to the results of Niehues SM.²¹ We assume that higher average values of the liver tissue density in our study is due to the significant number of the studied specimen were affected diffuse disease or focal lesions of the liver, that also affects the density of the liver tissue.

Comparison of the formulae

Table 3 lists used in this article formulae to calculate the volume of the liver. When analysing the dates of publications we can conclude that the problem of determining liver volume was actual in 1989 and remains relevant nowadays. Why in the daily practice of ultrasonographers these formulas do not apply, despite the high relevance of the liver size assessment? One of the answers to this issue can be found in the line "M" of table No. 3 (mean error of the formula). The average percent deviation from ALV varies from 23%¹⁶ to 56%.¹⁷ This is an unsatisfactory high values of the average percent error formula. The exception is the formula J Childs,¹⁴ which shows the minimum average deviation from actual volume (1%). However, the authors in their article¹³ point to the insufficient accuracy of the formula. This is caused in particular by the standard deviation of the average error. All the formulae in our study demonstrate similar hight variation up to 35% as well as the formula of J. Childs - 27% (Table 3). We should also note that all the formulae can give quite a large error in a big way. This is unacceptable from a diagnostic point of view. According to this parameter formula of Childs JT,¹⁴ is significantly, 1.66-2.23 times better than the other formulae.

Table 3 Shows the most common formulas of the liver volume calculation based on the clinical ultrasound measurements

$V = 133,2 + 0,422 \times CCRL \times APRL \times TransL$	M. Zoli (1989)
$V = (CCRL \times APRL \times TransL - 545) / 2320$	M. Patlas e.a. (2001)
$V = (0,12 + CCRL \times APRL \times TransL) / 2,55$	D. Glenn e.a. (1997)
$V = 320,86 + 0,317 \times CCRL \times APRL \times TransL$	D. Elstein e.a. (1997)
$V = 345,71 + 0,84 \times \max CCRL \times APRL \times APLL$	J. Childs e.a. (2014, 2016)

(CCRL, cranio-caudal diameter of the right lobe; APRL, antero-posterior diameter of the right lobe; TransL, transversal diameter of the liver; maxCCRL, maximal cranio-caudal diameter of the right lobe; APRL, antero-posterior diameter of the left lobe. All dimensions are in centimeters).

The second answer to the question why CLV formulae are not used in clinical ultrasound, is due to technical difficulties and operator-dependence of the measurement process. Four of five CLV formulae listed in table 1 use width of the liver as one of the arguments of the equation. Fig. 3 demonstrates the method of measurement of the width of the liver on the specimen. To measure TransL through clinical ultrasound using convex probe in most cases is impossible (Figure 4). Even when liver has a normal size its lateral borders are outside of the working area of the monitor screen. From this point of view, the bias of TransL measurement in clinical ultrasound is unsatisfactory high.

Figure 4 A: Ultrasound cross section of the liver trough subcostal access. TransL, width of the liver measured in horizontal plane (TransL), KPP, oblique transverse diameter (the most remote point of the right dome of the diaphragm and the left border of the liver). B: The same image. The borders of the liver are outlined. The TransL (TransL) do not fit in the image.

After publication of JT Childs,^{13,14} new volumetric formula has appeared. Liver volumetry now does not require additional time and special training of sonographer, because new volumetric equation consist in three simple liver diameters and does not use TransL. These liver measurements are recommended in last training course for clinical ultrasound and are included in ultrasound protocol (EFSUMB).

The next reason why volumetric formulae for calculation liver volume are not widely used in clinical ultrasound, is the lack everywhere spread of automated logging of the results of the ultrasound. Surely, the calculation of the liver volume on the calculator is an unacceptable complication of a routine process of logging of the clinical ultrasound results. The liver volumetric formulae should be built in automated workstation and in ultrasound equipment.

Figure 5 demonstrates a screenshot of the automated module for the liver volume assessment we have proposed to include in automated workstation for clinical ultrasound “Assistant.” We believe that the built-up of liver volumetric formulae in ultrasound equipment is an important factor for the objectiveness of the liver size estimation in clinical ultrasound.

Estimation of the liver volume

In present study we did not carry out to estimate the “normality” of the liver volume. We suppose the optimal formula must be able to accurately calculate the volume of the normal liver, and also of enlarged or reduced liver. Determination of the standard ranges of the liver volume, including constitutional features of the patients, is a topic of further research.

It is interesting to compare the actual liver volume with the standard liver volume. Unfortunately, in our study for technical reasons it was not possible to weigh the cadaver. In this regard, it is impossible to calculate the standard liver volume due to the lack of data on body weight. Earlier in our article,²⁶ a comparative analysis of the accuracy of 14 published formulae of the standard liver volume calculation was carried out.^{16,27,28} There is a perception that on the amount of the standard liver volume racial-ethnic and territorial-geographical factors are influenced. This is because the formulae for calculating standard liver volume are based on anthropometric data, which have ethno-territorial dependence. In work,²⁶ it was shown that the most accurate calculation formula of standard liver volume for use in conditions of the Kaliningrad region of the Russian Federation is the formula Chouker A.²⁷ This formula can be recommended as a reference evaluation for estimation CLV according to J. T. Childs. As the results of present study, we propose to include the formulae of JT Childs¹⁶ & A Chouker²⁷ into the clinical ultrasound protocol to calculate the volume of the liver and its reference evaluation.

Conclusion

- The average weight of liver as the results of post-mortem weighing is 1607 ± 562 g.
- The average liver volume determined by the water displacement method, is 1434 ± 503 ml.
- The average density of liver tissue is 1.14 ± 0.16 g/ml.
- The average calculated liver volume according to the formulae Glenn D,¹⁷ Zoli M,¹⁵ Patlas M,¹⁶ Elstein D.¹⁸ and Childs JT,¹⁶ amounted to 2259 ± 979 , 1851 ± 709 , 1754 ± 725 , 2147 ± 791 and 1355 ± 487 ml, respectively.
- The optimal formula to calculate liver volume in terms of the least deviation from the actual liver volume is Childs JT^{12,13} formula.

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Conflict of interest

The author declares that there is no conflict of interest.

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