Factors Affecting Liver Size

A Sonographic Survey of 2080 Subjects

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Objective. We sought to determine the size of the liver in a nonselected population sample to establish normal and reference values and to study potential factors influencing liver size. ***Methods.*** A total of 2080 subjects (983 male and 1097 female; age range, 18–88 years) underwent prospective ultrasound examination to determine the size of the liver. Subjects also underwent physical examination and completed a short standardized interview questionnaire covering potential factors influencing liver size. Data were evaluated descriptively. The influence of multiple variables on liver size was studied by means of a covariance analysis. ***Results.*** The average measured liver diameter (midclavicular line) ± SD was 14.0 ± 1.7 cm (median, 13.9 cm; range, 9.4–21.3 cm; average in male subjects, 14.5 ± 1.6 cm; and average in female subjects, 13.5 ± 1.7 cm). Results of the multivariate analysis showed that the factors body mass index, body height, sex, age, and (in male subjects) frequent alcohol consumption exert an influence over liver size measured at the midclavicular line. ***Conclusions.*** The sonographic measurement of liver size at the midclavicular line was shown to be an easy and practical method for routine use. Only in 239 (11.5%) of 2080 subjects did the size of the liver measured at the midclavicular line exceed 16 cm. Body mass index and body height are the most important factors associated with the diameter of the liver measured at the midclavicular line. ***Key words:*** alcohol; body height; liver; normal value; size; sonography.

Abbreviations
BMI, body mass index; MCL, midclavicular line

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Sonography has become very popular and is the most widespread diagnostic technique for examination of the liver.[1–3] Regarding the size of the liver, however, a uniform method of measurement has yet to be defined. Current knowledge of normal size is based on small surveys[4,5] and highly selected populations[6] or was derived from autopsy studies.[7] Furthermore, the effects on liver size of anthropometric factors and other variables, such as alcohol consumption, in nonselected populations have remained practically unassessed.

In addition to radiologic and computed tomographic methods, a number of sonographic methods for determining liver volume have been developed in recent years.[8,9] To date, several studies have tested the efficacy of different methods for determining liver volume.[10,11]

Because of the time required, however, sonographic determination of liver volume remains unsuitable for routine diagnostic applications and is reserved for specific clinical situations. The three-dimensional volume of the liver is difficult to quantify in terms of a single measurement parameter. Routine clinical assessment, however, demands a simple and reliably reproducible measurement method. One of the most commonly applied methods of estimating liver size in routine diagnostic situations is measurement of the liver diameter in the midclavicular line (MCL).[12]

The objective of this prospective screening survey was to measure the diameter of the liver in the MCL, to establish normal values for the population sampled, and to determine the influence of sex, height, body mass index (BMI), and alcohol consumption on liver size.

Materials and Methods

Sonographic surveys of the liver were performed in subjects residing in a rural community in southwestern Germany. Data were obtained as part of a prospective sonographically based screening survey for detection of *Echinococcus multilocularis* in an area recognized as endemic for *E multilocularis*.[13] All inhabitants were informed about our study via the local news media, by handbills, and at meetings. All residents 6 years of age and older were invited to participate in the study. For measurement of liver size, only participants 18 years of age and older were included. Sixty-seven percent (n = 2080) of the inhabitants who were 18 years of age and older (average age ± SD, 44.2 ± 16.0 years; range, 18–88 years) participated in the study. After approval by the Ethics Committee, written consent was obtained from all participants.

In addition to the ultrasound examinations, subjects' demographic data and medical histories, including information regarding lifestyle, were assessed with the use of a short questionnaire. Although the questionnaire included general socioeconomic questions (marital status, education, and occupation), the main focus was documentation of daily habits, such as the frequency of alcohol consumption.

The subjects' body heights and weights were obtained, and the BMI was calculated by the following formula: BMI = weight (kilograms)/height (meters)^2.

Ultrasound examinations were carried out by 8 assistants of the University Hospital of Ulm in 4 cubicles, where examinations were performed simultaneously. All personnel had been trained by the same experienced ultrasound examiner before the study, and this examiner was present in the examination room to provide a second opinion in cases in which the primary examiner could not give a definite diagnosis. More detailed information has been published previously.[14]

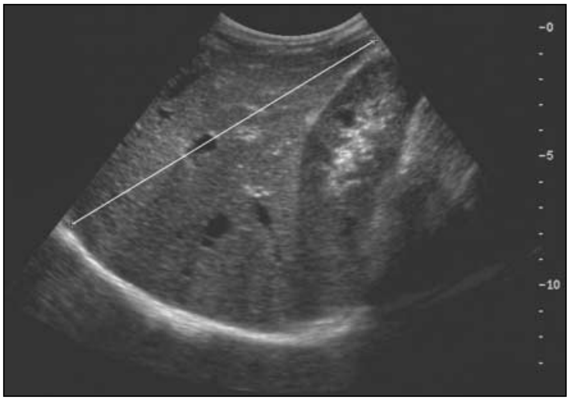
Sonographic Examinations

Examinations were carried out with the subjects in the supine position. For better access to the liver, subjects were instructed to raise their right hand behind their head, thus increasing the intercostal spaces and the distance from the lower costal margin to the iliac crest. The examination was carried out during deep inspiration and with a relaxed abdominal wall. In each case, the liver was examined in 3 planes, visualized longitudinally, cross-sectionally, and diagonally.

The size of the liver was measured in the right MCL (with measurement from the hepatic dome to the inferior hepatic tip) according to the method described by Börner et al[15] (Fig. 1). Before the ultrasound examinations, the participants had fasted for an average of 4.3 ± 2.9 hours (median, 4.0 hours; range, 0–19 hours). The ultrasound examinations were carried out on a Sonoline 400 system with a 3.5-MHz curved array probe (Siemens AG, Erlangen, Germany), an Ultramark 9 HDI unit, or 2 Apogee 800 units, all with 3.5- and 5.0-MHz transducers (Philips Medical Systems, Bothell, WA).

Statistics

Statistical evaluation of the data was descriptive. The distribution of qualitative characteristics was displayed with absolute and relative frequencies. For quantitative characteristics, such as age, mean ± SD, median, minimum, and maximum were determined. A multiple covariance analysis evaluated the influence of a given parameter on the diameter of the liver adjusted for other observed variables. By this method, the average increase in liver size per unit in cases of continuous variables (height, age, and BMI) and the adjusted mean of the liver diameter in cases of discrete variables were given. Statistical significance was assigned at $P < .05$.



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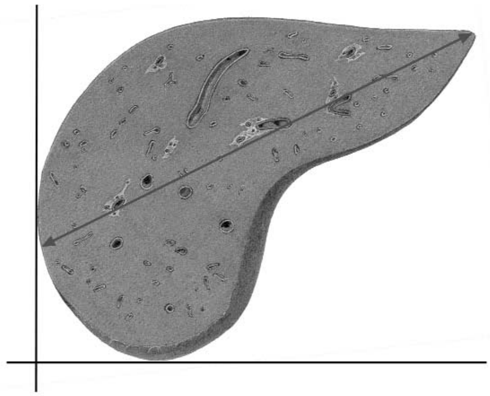

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Figure 1. Measurement of liver size in the largest craniocaudal diameter in the MCL during inspiration in a supine subject. **A**, Sonographic measurement. **B**, Diagrammatic representation of measurement.

Results

The average diameter of the liver measured in the MCL in the total collective was 14.0 ± 1.7 cm (median, 13.9 cm; range, 9.4–21.3 cm). Distribution of liver size in the collective showed that 74.1% of subjects (n = 1541) had liver diameters of 15 cm or less, whereas 14.4% (n = 300) had liver diameters of greater than 15 to 16 cm, and 11.5% (n = 239) had diameters of greater than 16 cm. The distribution of liver diameters measured in the MCL for the total collective is presented in Figure 2.

Univariate Analysis of Potential Factors

Age and Sex

When age was considered by itself, a definite association between liver size and age was observed in the 2080 subjects examined. To represent this association better, the ages of the subjects are broken down into 6 groups (Table 1).

For female (n = 1097) and male (n = 983) subjects, the average liver diameters measured in the MCL were 13.5 ± 1.7 cm (median, 13.4 cm; range, 9.4–19.9 cm) and 14.5 ± 1.6 cm (median, 14.5 cm; range, 10.0–21.3 cm), respectively ($P < .001$).

Height and BMI

The mean height of 2074 subjects stood at 170.7 ± 9.3 cm; for men (n = 982) it was 177.3 ± 7.1 cm; and for women (n = 1092) it was 164.8 ± 6.7 cm. The mean body weight of 2075 subjects was 76.9 ± 14.5 kg; for men (n = 981) it was 83.7 ± 12.3 kg; and for women (n = 1094) it was 70.8 ± 3.5 kg. The BMI was calculated in 2073 subjects (99.7%). Subjects were assigned to 1 of 3 groups on the basis of BMI. Persons considered to be of ideal weight had an average liver size of 13.1 ± 1.4 cm (median, 13.1 cm; range, 9.5–16.7 cm), whereas those of normal weight had an average liver size of 13.5 ± 1.5 cm (median, 13.5 cm; range, 9.4–18.4 cm), and overweight subjects had an average liver size of 14.5 ± 1.7 cm (median, 14.4 cm; range, 10.2–21.3 cm; Table 2).

Alcohol Consumption

Data with respect to the frequency of alcohol consumption were obtained from 2078 (99.9%) of the 2080 subjects surveyed. Subjects were assigned semiquantitatively to 1 of 3 groups. Group 1 included 1204 subjects (57.9%) reporting no or only infrequent (once per week or less) alcohol consumption. Group 2 consisted of 507

Figure 2. Distribution of liver diameters in the MCL in the total collective; 1 indicates male; and 2, female.

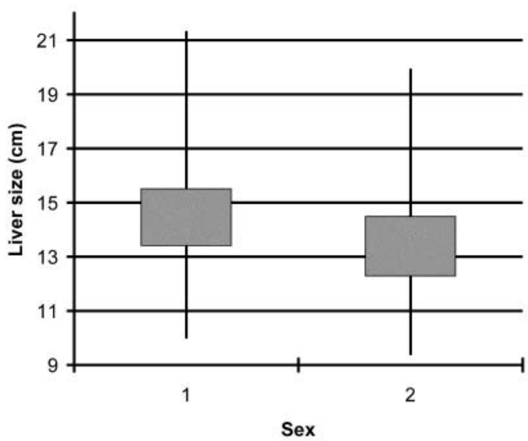

Table 1. Liver Diameter in the MCL in Individual Age Groups

Age, y	n (%)	Liver Diameter, cm Mean ± SD	Liver Diameter, cm Median (Range)
18–25	250 (12.0)	13.6 ± 1.5	13.4 (9.5–17.2)
26–35	514 (24.7)	13.7 ± 1.6	13.6 (10.0–18.5)
36–45	402 (19.3)	14.0 ± 1.6	14.0 (9.4–18.8)
46–55	308 (14.8)	14.2 ± 1.7	14.1 (10.2–19.9)
56–65	343 (16.5)	14.4 ± 1.8	14.4 (10.6–19.8)
≥66	263 (12.7)	14.1 ± 2.0	14.0 (10.0– 21.3)
Total	2080 (100.0)	14.0 ± 1.7	13.9 (9.4–21.3)

subjects (24.4%) who consumed alcohol several times per week but not every day. Finally, group 3 included 367 subjects (17.7%) reporting daily consumption of alcohol (Table 3).

The diameter of the liver in the MCL in subjects with no or only infrequent alcohol consumption (group 1) averaged 13.7 ± 1.7 cm versus 14.3 ± 1.6 cm in the groups with regular alcohol consumption (groups 2 and 3). Corresponding to the higher frequency of alcohol consumption, an increase in the average diameter of the liver was observed, from 13.7 ± 1.7 cm in group 1 to 14.1 ± 1.5 cm in group 2 and 14.6 ± 1.7 cm in group 3 (Table 3).

Simultaneous Assessment of Several Factors

At simultaneous evaluation of the effects of several factors on a variable of interest (target variable), the effect of each factor was adjusted for the potential confounding effects of the other factors.

This analysis showed that age as an influence parameter with regard to the diameter of the liver in the MCL shows a tendency toward an increase with age ($P = .003$). When seen in terms of the average increase in the size of the liver per year (0.007 cm/y), this association is not clinically relevant.

Multiple analysis revealed a correlation of liver diameter in the MCL with sex. Male subjects had a larger mean diameter in the MCL (14.2 cm after adjustment) than did female subjects (13.9 cm after adjustment; $P = .006$). It follows that sex can be ignored as a clinically relevant influence parameter.

In both the univariate and multiple analyses, height was shown to be a significant influence parameter affecting liver size in the MCL ($P < .001$). Liver diameter increases by approximately 0.04 cm/cm of height. Thus, height can be considered a moderately important factor influencing liver diameter in the MCL (Table 4).

Both univariate and multiple analyses showed an influence of BMI on liver diameter in the MCL ($P = .001$). An average increase of 0.16 cm/kg per m^2 (after adjustment) in the BMI underscores the importance of BMI as a predictor of liver diameter in the MCL (Table 4).

A correlation between reported increased frequency of alcohol consumption and liver diameter was observed in male subjects ($P = .026$), although with only a slight variation in the mean liver diameter between the different consumption classes. A corresponding correlation could not be shown in the female subjects ($P = .7$; Table 4). However, the influence of the frequency of alcohol consumption on liver size also appeared to be fairly slight in the male subjects.

Discussion

Diagnostic imaging techniques are superior to clinical examination in determining the size of the liver.[5,16] To date, however, there is a paucity of data regarding normal and borderline values, and no uniform procedure for measuring the size of the liver has been established that can serve as a guideline for ultrasound examination

Table 2. Liver Diameter in the MCL in Individual BMI Classes

BMI Class	n (%)	Liver Diameter, cm Mean ± SD	Liver Diameter, cm Median (Range)
I	213 (10.3)	13.1 ± 1.4	13.1 (9.5–16.7)
Male, BMI < 22 kg/m^2			
Female, BMI < 21 kg/m^2			
II	753 (36.3)	13.5 ± 1.5	13.5 (9.4–18.4)
Male, 22 kg/m^2 ≤ BMI ≤ 26 kg/m^2			
Female, 21 kg/m^2 ≤ BMI ≤ 25 kg/m^2			
III	1107 (53.4)	14.5 ± 1.7	14.4 (10.2–21.3)
Male, BMI > 26 kg/m^2			
Female, BMI > 25 kg/m^2			

Table 3. Liver Diameter in the MCL in Relation to Frequency of Alcohol Consumption

Alcohol Consumption Class	n (%)	Liver Diameter, cm Mean ± SD	Median (Range)
I, maximum once/wk	1204 (57.9)	13.7 ± 1.7	13.6 (9.4–19.9)
II, multiple times/wk but not daily	507 (24.4)	14.1 ± 1.5	14.0 (10.3–19.6)
III, daily	367 (17.7)	14.6 ± 1.7	14.6 (10.4–21.3)

of the liver. The method used in this study was oriented to the method described by Börner et al.[15] Comparison of sonographic measurements of liver diameter in the right MCL with those compiled from autopsy studies showed good correlation between sonographic findings and data obtained from autopsy.[4]

In our collective, the average diameter of the liver measured in the MCL stood at 13.9 ± 1.7 cm. In 74.1% of subjects, the diameter of the liver was 15 cm or less. In a study published by Gosink and Leymaster,[4] data regarding the liver obtained at autopsy were correlated with anthropometric data of the respective patient, and this correlation was used to make the diagnosis of hepatomegaly. These findings were then compared with sonographic measurement data obtained from the same patients during examinations conducted shortly before death. In cases in which the sonographically measured liver diameters were 13 cm or less, 93% of livers were considered of normal size, whereas in cases in which sonography returned findings of liver diameters of 15.5 cm or greater, autopsy findings in connection with anthropometric data permitted diagnosis of hepatomegaly in 75% of individuals studied.[4] The estimation of liver size on the basis of a single parameter, such as liver diameter in the right MCL, is limited by various hepatic morphotypes.[17] This requires a different orientation of the liver in very obese (>95 kg) and very light (<50 kg) persons, necessitating the reporting of further parameters for determination of liver size.[6]

To our knowledge, no studies have been published to date that have sonographically examined influence parameters in a correspondingly large collective. Our data show that both height and BMI are significant factors that influence liver diameter in the right MCL. A correlation between organ size and weight in anthropometric findings (height, BMI, body surface area, and chest dimensions) is supported by both sono-

Table 4. Factors Influencing Liver Size

Factor	Liver Size, cm Mean Increase/Unit (95% CI)	Mean (95% CI)	*P**
Height	0.042 (0.032–0.052)	NA	<.001
BMI	0.162 (0.147–0.178)	NA	<.001
Age	0.007 (0.002–0.011)	NA	.003
Sex			
Female	NA	13.9 (13.8–14.0)	.006
Male	NA	14.2 (14.1–14.3)	
Alcohol consumption			
Total sample			
Never/rarely	NA	13.9 (13.8–14.0)	.034
Sometimes	NA	14.0 (13.8–14.1)	
Daily	NA	14.2 (14.0–14.3)	
Female			
Never/rarely	NA	13.5 (13.4–13.6)	.7
Sometimes	NA	13.6 (13.4–13.9)	
Daily	NA	13.6 (13.2–13.9)	
Male			
Never/rarely	NA	14.3 (14.2–14.5)	.026
Sometimes	NA	14.4 (14.3–14.5)	
Daily	NA	14.6 (14.5–14.8)	

CI indicates confidence interval; and NA, not applicable.
*Simultaneous analysis; for univariate analysis, $P < .001$.

graphic studies[6,8,18,19] and by studies based on autopsy findings.[7] The findings of this study suggest that BMI exerts a greater influence on liver size than does height.

Earlier studies reported that liver size decreases with age.[6,7] That finding was not confirmed in our collective. The well-known phenomenon that male gastrointestinal organs are larger than female organs has been documented in studies using diagnostic imaging techniques.[8,20,21] Our data also showed an absolute size difference between female and male subjects (13.5 versus 14.5 cm). Adjusted for other anthropometric factors (height and BMI) and alcohol consumption, however, this difference is not clinically relevant (mean values adjusted for other parameters, 13.9 versus 14.2 cm).

A survey of the subjects' alcohol history for use in estimating the influence of regular alcohol consumption on liver size is difficult in a large collective such as the one in this study. Improving the measurement of consumption has remained one of the most elusive goals of alcohol research.[22] The participants in our collective reported a relatively high rate of consumption of self-produced alcoholic beverages (must). Because these beverages do not have a defined alcohol concentration, we did not attempt to determine the absolute amounts of alcohol consumed, which certainly reduced the strength of these data. An adequate evaluation of all relevant facets of this problem, including the duration, frequency, and absolute amount of alcohol consumed, is, in our opinion, practically impossible to conduct in a collective as large as ours; hence, we settled for the current frequency of alcohol consumption as the most easily surveyed parameter.

In this study, participants with regular alcohol consumption had increased liver diameters measured in the right MCL in comparison with those with no or only infrequent alcohol consumption, even when adjusted for other factors. When male and female subjects were taken separately, however, this difference was observed only for the former, which confirmed observations reported by Andersen et al.[20] One possible explanation for this phenomenon could be the consumption of lower absolute amounts of alcohol by female drinkers, although this was not quantified in our present study. Another study that focused on this question found hepatomegaly in persons with high alcohol consumption over the previous 2 years.[23] In a comparison study, sonographic determination of liver size was not a good parameter for recognizing persons with increased alcohol consumption.[24] The only slight difference in liver diameter between the different groups observed in our collective suggests that the influence of the frequency of alcohol consumption on liver diameter is slight even in the male subgroup. A final evaluation of alcohol as an influence parameter, however, must include not only the frequency of alcohol consumption but also the absolute amount of alcohol consumed and the pattern of drinking.

On the basis of the results of this study, we suggest that a sonographic finding of a liver diameter of 16 cm or greater in the right MCL should be considered consistent with enlargement of the liver. Influence parameters, particularly BMI and height, must be considered individually in borderline cases. The influence of special factors such as alcohol consumption on liver size must be addressed specifically by further studies in representative collectives.

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