3D Volumetric Measurement of Normal Pediatric Livers: Creating a Reference Database and Predictive Model

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Introduction

Accurate and reproducible measurements of pediatric organs are necessary for defining normal organ volume, size, growth rates, and patterns of development, which aids in determining pathological variants. Currently, no modern reliable database exists for normal liver volume (LV) in children. Several equations have been proposed to predict normal LV in children[1], however, many of these formulas are based on adult data or are derived from small samples and have not taken advantage of the most advanced technology in determining LV from imaging in vivo.

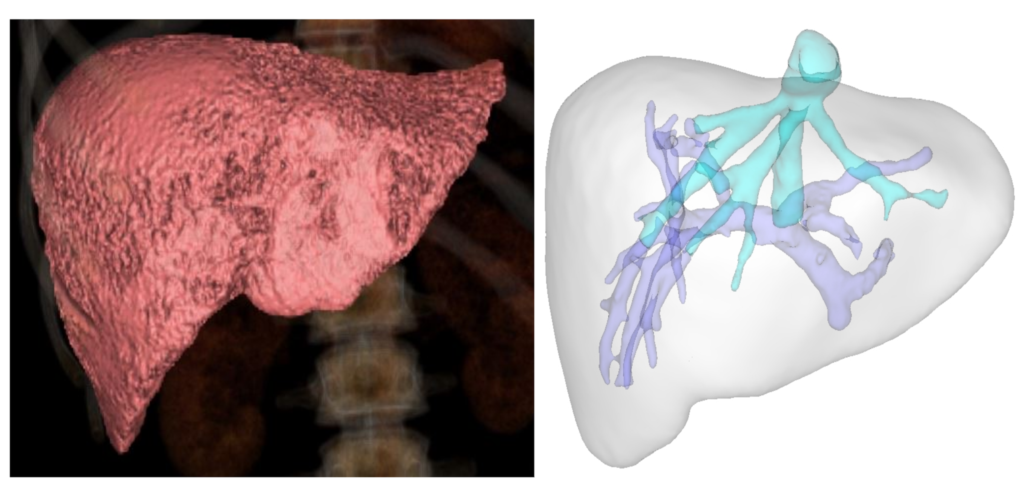

Figure 1: 3D rendered and segmented liver CT data

Research Questions

What is normal LV in children? Should normal LV be divided into normative values in children based on gender, age, weight (wt) kg, height (ht) cm, body surface area (BSA) m^2, body mass index (BMI), or on a combination of these parameters? Is it possible to predict LV in children using these parameters?

Materials and Methods

This study is a retrospective review of normal contrast enhanced abdomen and pelvis CT images, performed between 1/1/16 – 2/28/17, identified within the Phoenix Children's Hospital picture archive communications system (PACS), following Institutional Review Board (IRB) approval. The cohort of 179 patients included 89 female (49.7%) from 1 month – 18 years. Gender, age, wt, and ht were recorded for each patient; BSA and BMI were calculated (*Table 1*). LV measurements were obtained using segmentation images software (IntelliSpace, Phillips Healthcare, Haifa, Israel) where the liver is colorized and LV was automatically calculated (*Figure 1*).

Statistical Analysis

Univariate linear regression was used to independently associate each covariate with total LV. Each variable was entered in a second linear regression model where a backwards stepwise variable selection determined the best covariates that predicted total LV (*Figures 2 & 3*). The final model was stratified by age to ascertain whether age modified the predictive capabilities of the covariates. The stratified models were further stratified by gender to assess gender's role in effect modification. All p-values were 2-sided and $p < 0.05$ was considered statistically significant.

Results

Univariate analysis of LV was most strongly correlated with and predicted by BSA ($R^2 = 0.90$, $p < 0.0001$), which could be defined by: LV = -123.6 + 953.8*BSA (*Figure 4*).
In multivariate analysis BSA, gender ($p = 0.02$), and ht ($p = 0.003$) were the covariates that best predicted LV (*Table 2*). Stratifying the model by age did not modify the predictive capabilities of the covariates. Further stratifying by gender did demonstrate inconsistent effect modification in some age groups.

Variables N=179	Values (mean, SD)
Age At Exam	109 (62.6)
Weight, kg	38.9 (26.3)
Height, cm	130.4 (32.2)
BMI, kg.m^2	20.0 (6.35)
BSA, m^2	1.15 (0.52)

Table 1: Descriptive statistics

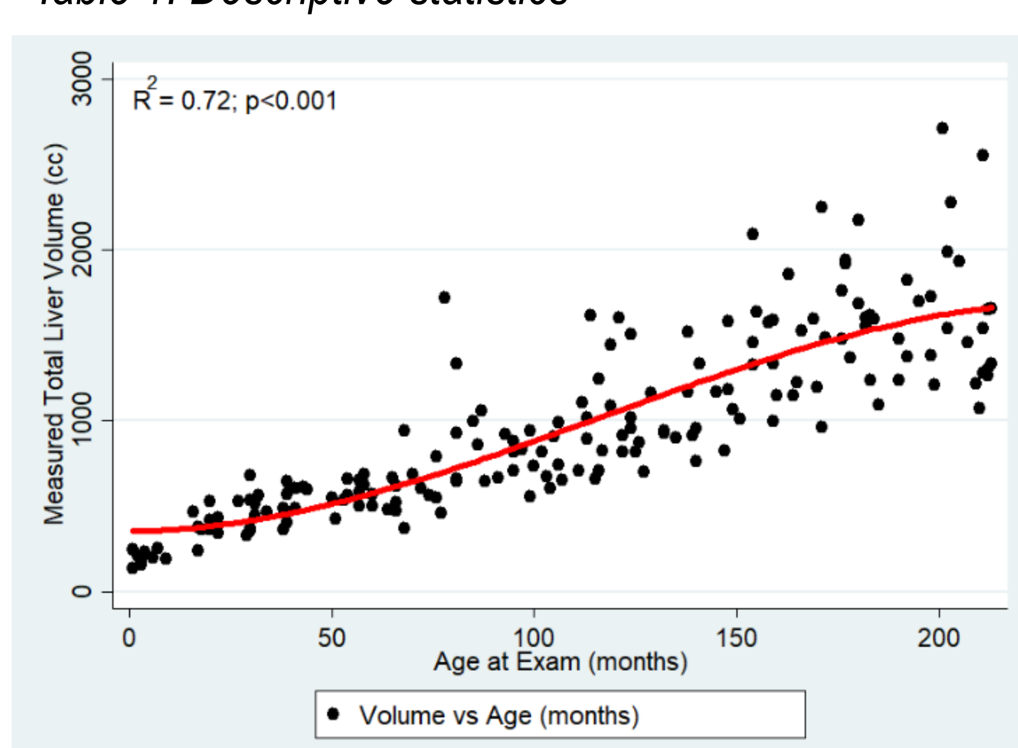

Figure 2: Univariate linear regression of LV vs. age

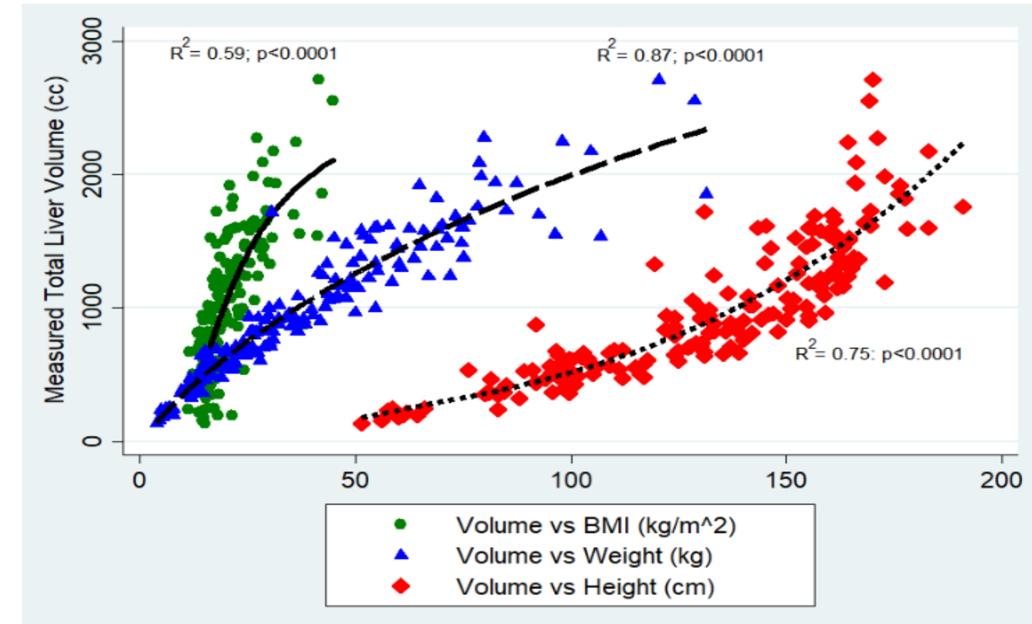

Figure 3: Univariate linear regression of LV vs. BMI; LV vs. wt; LV vs. ht

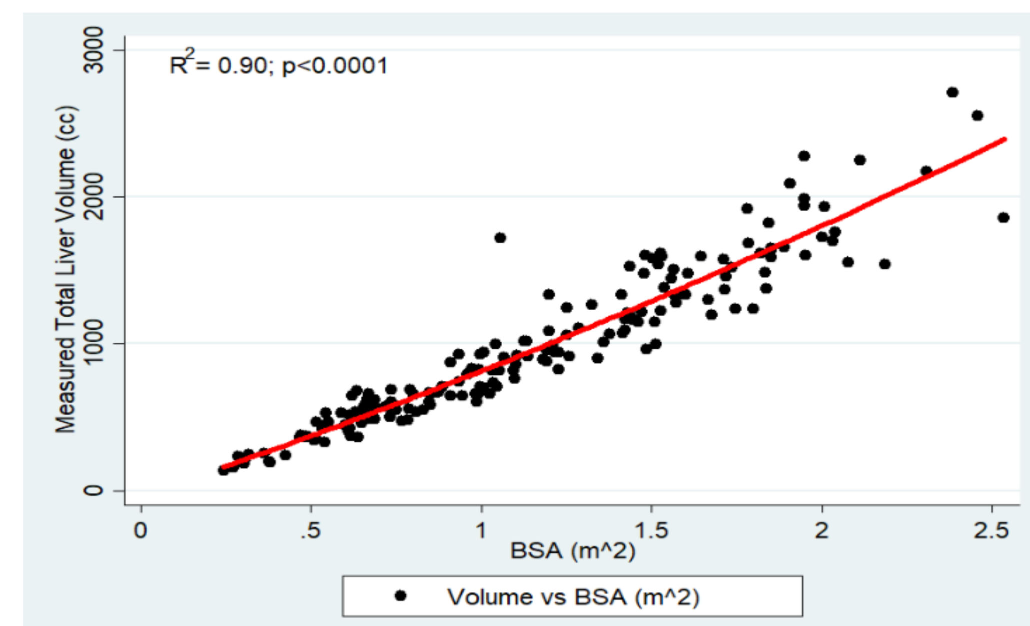

Figure 4: Univariate linear regression of LV vs. BSA

Variables	Beta (95%CI)	p-value	Adjusted R^2
Overall			
BSA	**1145.2** (1011.9, 1278.4)	<0.0001	0.90
Gender (female)	**-60.7** (-109.9, -11.5)	0.02	
Height	**-3.26** (-5.41, -1.11)	0.003	
< 5 years of Age (n=48)			
BSA	**906.1** (358.8, 1453.3)	0.002	0.79
Gender (female)	**-48.5** (-92.1, -4.89)	0.03	
Height	**-0.44** (-5.39, 4.50)	0.86	
5 – 9 years (n=51)			
BSA	**1448.3** (1071.8, 1824.7)	<0.0001	0.71
Gender (female)	**-79.0** (-168.8, 10.8)	0.08	
Height	**-6.82** (-13.1, -0.55)	0.03	
10 – 15 years (n=48)			
BSA	**1105.9** (815.6, 1396.4)	<0.0001	0.75
Gender (female)	**21.7** (-95.4, 138.7)	0.71	
Height	**-2.99** (-8.97, 2.98)	0.32	
> 15 years (n=32)			
BSA	**1080.2** (722.9, 1437.5)	<0.0001	0.68
Gender (female)	**-166.4** (-343.3, 10.5)	0.06	
Height	**2.23** (-12.2, 16.7)	0.75	

Table 2: Multivariate linear regression of each covariates with subsequent stratification by age

Variables	Males only		Females only	
	Beta (95%CI)	p-value	Beta (95%CI)	p-value
Overall				
BSA	1188.5 (979.5, 1397.5)	<0.0001	1110.6 (937.3, 1283.9)	<0.0001
Height	-3.71 (-7.01, -0.42)	0.03	-2.88 (-5.73, -0.04)	0.047
< 5 years				
BSA	**1094.0** (2.37, 1950.6)	0.02	**731.8** (-15.3, 1478.9)	0.054
Height	**-2.80** (-10.8, 5.21)	0.48	**1.42** (-5.19, 8.05)	0.65
5 – 9 years				
BSA	**1348.6** (557.7, 2139.4)	0.002	**1517.2** (1183.2, 1851.3)	<0.0001
Height	**-3.17** (-16.3, 9.93)	0.62	**-9.34** (-14.9, -3.76)	0.002
10 – 15 years				
BSA	**902.1** (556.4, 1247.8)	<0.0001	**1585.3** (1029.3, 2141.4)	<0.0001
Height	**-0.17** (-6.79, 6.45)	0.95	**-10.7** (-27.4, 6.05)	0.19
> 15 years				
BSA	**1515.5** (906.4, 2125.2)	<0.0001	**831.9** (367.7, 1296.2)	0.002
Height	**-7.81** (-27.0, 11.4)	0.38	**10.9** (-16.1, 37.9)	0.40

Table 3: Gender stratification of multivariate linear regression described in Table 2

Conclusion

This study addresses a gap in medical literature by obtaining in vivo 3D volumetric measurements of normal pediatric LV using a large sample size. Although other predictive models to calculate LV have been created, the aforementioned power of this project would suggest improved accuracy. This data has many clinical applications, most notably in surgical planning for liver transplantation and in diagnosis of hepatic enlargement in liver disease. Our study did not stratify by ethnicity; calling for additional studies to analyze this factor.

Summary

This equation may be used in clinical applications to predict normal LV in children:

LV = -123.6 + 953.8*BSA

Acknowledgements

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1. Johnson, TN et al., Changes in liver volume from birth to adulthood: A meta-analysis. Liver Transplantation 2005; 12; (11): 1481-1493.