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QUANTITATIVE ASSESSMENT OF SEVERITY OF CIRRHOSIS WITH LIVER AND SPLEEN INDICES MEASURED USING MULTIDETECTOR COMPUTED TOMOGRAPHY

Radio-Diagnosis

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ABSTRACT

Child-Pugh and MELD scores generally serve as the gold standard for prognostication of cirrhosis but has limitations. This study employs non-invasive volumetric parameters like RV (Right lobe liver volume),SV (spleen volume) and RV/SV (Right lobe liver to spleen volume ratio) for determining severity of cirrhosis with MDCT as the imaging method of choice. Philips iCT256 Slice CT Intellispace Portal Workstation volume computation software was used to determine volume in 105 cirrhotic patients. The volumetrics of different CHILD grades will be compared statistically to determine any association. With increasing Child-Turcotte-Pugh scores, RV and RV/SV tend to decrease ($p=0.004$ and $p<0.001$ respectively) and SV tend to increase ($p=0.005$) respectively. Among these parameters, RV/SV was the best noninvasive factor for the assessment of severity of liver cirrhosis among Child-Pugh class A and B (AUC = 0.706), between A and C (AUC = 0.795), and between B and C (AUC=0.644).

KEYWORDS

Severity of cirrhosis, right lobe liver volume, spleen volume.

INTRODUCTION

Cirrhosis refers to the development of regenerating nodules encircled by fibrous bands as a result of life threatening chronic liver injury.(1) As the disease advances, this leads to portal hypertension, leaving patients at a high risk of developing potentially deadly side effects such as hepatic encephalopathy and hepatic failure. (2) Globally, chronic liver disease (CLD) have a considerable negative impact on morbidity and death.(1)

A standard approach for assessing the severity of chronic liver disease is Child-Turcotte-Pugh classification and a prognostic indication for ALF (acute liver failure) is the MELD (Model for end-stage liver disease) score.

To measure the liver function of people with cirrhosis and ALF, hepatic atrophy has been reported to be just as essential as serologic indices and laboratory data(3). Saygili et al. demonstrated the efficacy of cross sectional imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) for assessing the degree of cirrhosis caused by viral hepatitis.(4)

An excellent objective metric for estimating liver atrophy is volume, which also accurately predicts how patients with fulminant hepatic failure would fare.(5) Cirrhotic patients showed significantly lower total liver-to-spleen volume ratio, smaller total and functional liver volume, larger spleen volume when compared to healthy individuals. In patients with decompensated stages, these volumetric parameters showed significant alteration.(6)

AIM AND OBJECTIVES

The objectives were to assess the feasibility of combined volumetric assessment using both RV (Right lobe liver volume) and SV (spleen volume), for detecting the presence and severity of cirrhosis than doing so with either parameter alone. As a direct outcome of this, the detection and categorization of the same would become significantly more sensitive and accurate.

MATERIALS AND METHODS

This is a Cross-Sectional Prospective study. After obtaining approval from the Thesis Protocol Review Committee (Scientific, Ethical & Financial), Amrita Institute of Medical Sciences, this study was carried out. On a routine basis, prior to triple phase study an informed consent was taken from all the CLD patients before contrast administration.

Patient selection:

Patients diagnosed with cirrhosis based on laboratory investigations, physical examination, imaging findings were included in the study.

Exclusion criteria included 1)Recurrent history of GI bleed or active gastrointestinal bleeding; 2)Imaging features of hepatic artery-portal vein fistula and portal vein emboli;3)History of treatments for portal hypertension including transjugular intrahepatic portosystemic shunt, balloon occluded retrograde transvenous obliteration, beta blocker therapy, partial spleen embolization, endoscopic therapies and splenectomy; 4)Concomitant Hepatic Schistosomiasis;5)Primary haematological disorders and malignancies excluding hepatocellular carcinoma;6)Active alcohol abuse;7)History of any hepatic or splenic surgeries. Consequently, 105 samples were included in this study

Scanning parameters:

256 iCT Philips MDCT was used.A plain scan of the lower chest and upper abdomen was performed initially followed by a triphasic scan following an omnipaque injection.

A total dose 1.5 ml/kg with iodine concentration of 350 g/L via 18-gauge IV catheter over 25s using bolus tracking with triggering done at 100HU in the aorta at the aortic hiatus.Three sets of mages were taken in a craniocaudal orientation at 15(hepatic arterial phase), 25(portal), and 60 s (venous) in a single breath hold.

Using the Philips Intellispace Portal Workstation, CT volumetry was carried out. First, 5mm thick slice axial venous phase scans were subjected to a programme for automated liver extraction. Second, manual editing was done by radiologist using specifically created software tool on each slice of image to adjust the border. To improve volumetric measurement accuracy, major veins (including the extrahepatic portal vein and inferior vena cava) and major fissures were not included, including the ligamentum teres fissure.

After that, the spleen volume will be acquired in a manner analogous to that of the RV measurement by manually tracing the outline of spleen on the axial delayed phase images. The RV/SV ratio will be determined.

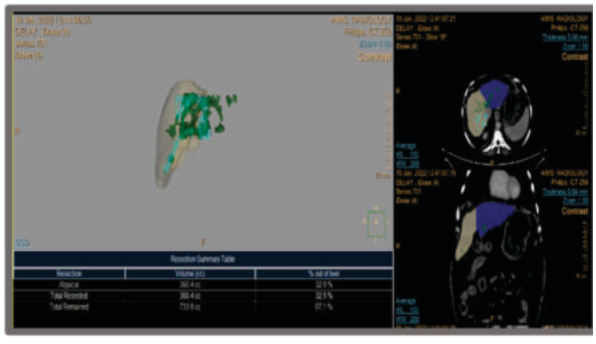

Figure 1: Graphical illustration of estimated 2D and 3D liver volumes and the written estimate of right lobe liver volume

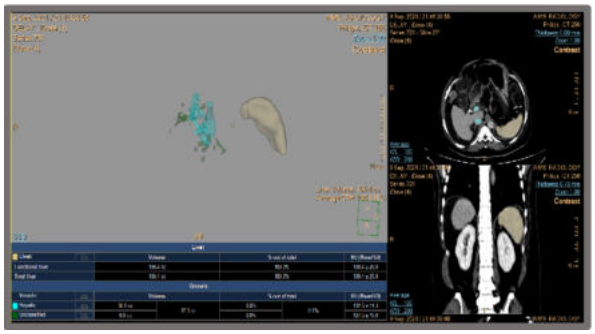

Figure 2: Graphical illustration of estimated 2D and 3D spleen volumes and the written estimate of spleen volume

RESULTS

In our study,105 patients diagnosed with chronic liver disease (CLD) were equally distributed between CHILD A,B and C.

The mean age group being 56.97 ± 8.11in CHILD A, 58.63± 9.78 in CHILD B and 51.43± 9.32 in CHILD C category.

The gender was equally distributed between three groups and there was no statistically significant difference in the population characteristics among the groups.

Comparison of RV (Right lobe liver volume), among the CHILD class, showed a mean±SD of RV 773.71±242.00 in CHILD A category, 670.98±308.40 in CHILD B category and 558.58±230.47 in CHILD C. The multiple comparison test shows a statistically significant RV between CHILD A and C with p value <0.001. (Figure 3A)

Table 1: Comparison of mean RV among CHILD A,B and C

Parameters	CHILD class Mean±SD			p value
	CHILD A (n=35)	CHILD B (n=35)	CHILD C (n=35)	
RV	773.71±242.00	670.98±308.40	558.58±230.47	0.004

Comparison of SV (spleen volume), among the CHILD class, showed a median(Q1,Q3) SV of 228.20 (185.40, 406.80) in CHILD A category, 335.90 (279.45, 461.45) in CHILD B category and 492.80(230.55, 631.65) in CHILD C category.The multiple comparison test shows a statistically significant SV between CHILD A and C with p value 0.002. (Figure 3B)

Table 2: Comparison of mean SV among CHILD A,B and C

CHILD Class	n	SV Mean±SD	Median (Q1,Q3)	p value
CHILD A	35	303.31±170.79	228.20 (185.40, 406.80)	0.003
CHILD B	35	386.91±201.88	335.90 (279.45, 461.45)	
CHILD C	35	493.83±316.38	492.80(230.55, 631.65)	

Comparison of RV/SV (Ratio of right lobe liver volume to spleen volume), among the CHILD class, showed a median(Q1,Q3) RV/SV of 2.55(1.52, 4.74) in CHILD A category, 1.88(1.07, 2.36) in CHILD B category and 1.45(0.87, 1.90) in CHILD C. The multiple comparison test shows a statistically significant RV/SV between CHILD A and B with p value 0.02 and between CHILD A and C category with a p value <0.001. (Figure 3C)

Table 3 : Comparison of mean RV/SV among CHILD A,B and C

CHILD Class	n	RV/SV Mean±SD	Median (Q1,Q3)	p value
CHILD A	35	3.417±2.186	2.55(1.52, 4.74)	<0.001
CHILD B	35	2.016±1.100	1.88(1.07, 2.36)	
CHILD C	35	1.523±1.034	1.45(0.87, 1.90)	

Out of 70 patients, RV between CHILD A and B (AUC 63.2%) was found to be statistically not significant with p value of 0.057.

Out of the 35 patients (AUC 64.2%) who had SV <308.8, 14(40%) belong to CHILD B. Whereas, out of the 35 patients who had SV>308.8, 21(60%) belong to CHILD B in the study period. The association of SV between CHILD A and B was determined to have a p value of 0.040 that was statistically significant.SV had a sensitivity of 60% and specificity of 60%. The positive predictive value was 60%, negative predictive value was 60% with accuracy of 60% Out of the 35 patients (AUC 70.6%) who had RV/SV<2.05 23 (65.7%) belong to CHILD B. Whereas, out of the 35 patients who had RV/SV>2.05, 12 (34.3%) belong to CHILD B in the study period. The association of RV/SV between CHILD A and B was determined to have a p value of 0.003 that was statistically significant. RV/SV had a sensitivity of 65.71% and specificity of 65.71%. The positive predictive value was 65.71%, negative predictive value was 65.71% with accuracy of 65.71%.(Fig 4)

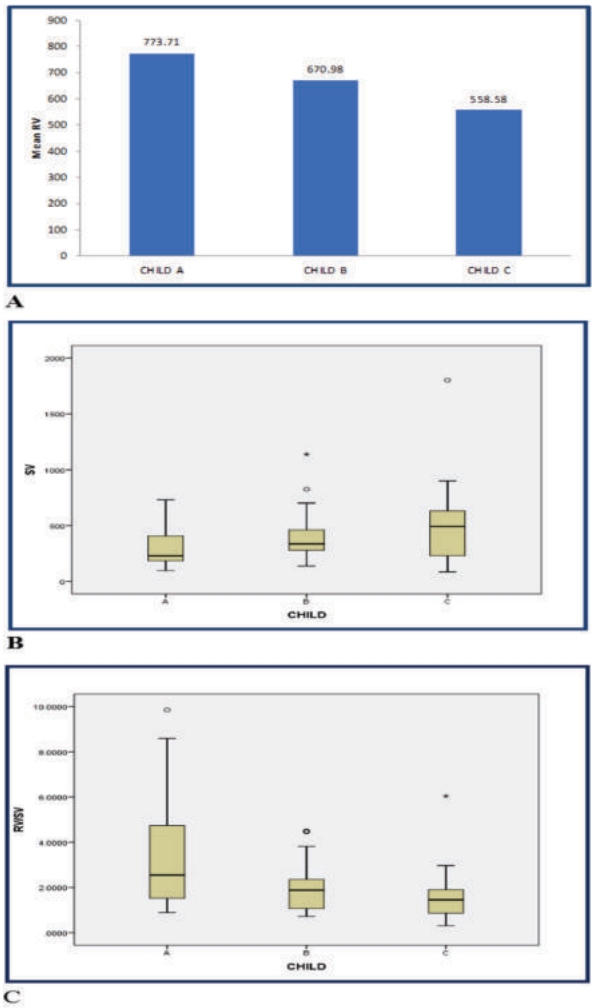

Figure 3: Comparison of mean RV(A), SV(B), RV/SV(C) among CHILD A,B and C

With AUC 70.6% and cutoff value 2.05, p value 0.003.

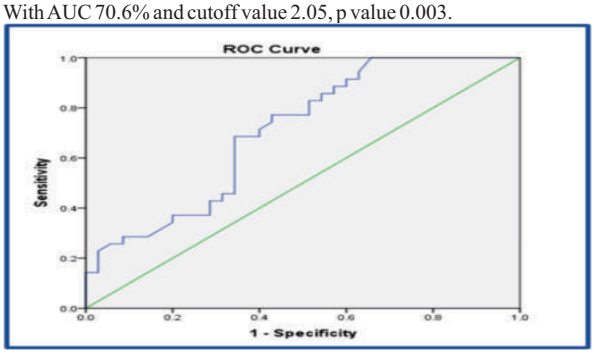

Figure 4:ROC of RV/SV between CHILD A and B

Out of 70 patients, RV between CHILD B and C (AUC 60.4%) was found to be statistically not significant with p value of 0.134.

Out of 70 patients, SV between CHILD B and C (AUC 61%) was found to be statistically not significant with p value of 0.113.

Out of the 35 patients (AUC 64.4%) who had RV/SV<1.67, 21(60%)

belong to CHILD C. Whereas, out of the 35 patients who had RV/SV>1.67, 14 (40%) belong to CHILD C in the study period. The association of RV/SV between CHILD B and C was found to be statistically significant with p value of 0.038. RV/SV had a sensitivity of 60% and specificity of 60%. The positive predictive value was 60%, negative predictive value was 60% with accuracy of 60%. (Fig 5)

Out of the 35 patients (AUC 76.7%) who had RV < 639.25, 25(71.4%) belong to CHILD C. Whereas, out of the 35 patients who had RV >639.25, 10 (28.6%) belong to CHILD C in the study period. The association of RV between CHILD A and C was found to be statistically significant with p value of <0.001. RV had a sensitivity of 71.43% and specificity of 71.43%.The positive predictive value was 71.43%, negative predictive value was 71.43% with accuracy of 71.43%.

With AUC 64.4% and cutoff value 1.67, p value 0.038.

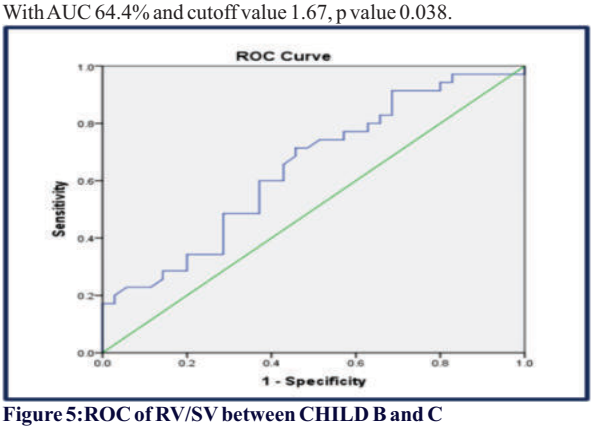

Figure 5:ROC of RV/SV between CHILD B and C

Out of the 35 patients (AUC 72.3%) who had SV< 321.75, 12(34.3%) belong to CHILD C. Whereas, out of the 35 patients who had SV>321.75, 23(65.7%) belong to CHILD C in the study period. The association of SV between CHILD A and C was found to be statistically significant with p value of 0.001. SV had a sensitivity of 65.71% and specificity of 65.71%. The positive predictive value was 65.71%, negative predictive value was 65.71% with accuracy of 65.71%.

Out of the 35 patients (AUC 79.5%) who had RV/SV< 1.79, 24(68.6%) belong to CHILD C. Whereas, out of the 35 patients who had RV/SV>1.79, 11 (31.4%) belong to CHILD C in the study period. The association of RV/SV between CHILD A and C was found to be statistically significant with p value of <0.001. RV/SV had a sensitivity of 68.57% ,specificity of 68.57%. The positive predictive value was 68.57%, negative predictive value was 68.57% with accuracy of 68.57%.(Fig 6)

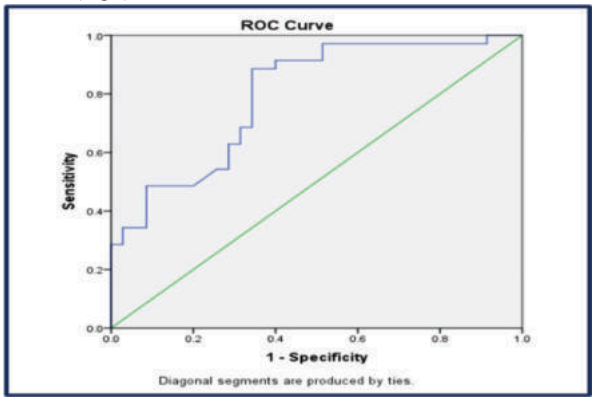

Figure 6:ROC of RV/SV between CHILD A and C

With AUC 79.5% and cutoff value 1.79, p value <0.001

DISCUSSION

Patel et al. in September 2021**,** conducted a study in Milan to investigate if measuring the volume of the liver and spleen could accurately predict the prognosis of cirrhosis patients using CT. The results of that investigation are comparable to the findings of our own study.(6)

Patients who were in a decompensated stage had significantly smaller liver volume, larger spleen volume and lower liver to spleen volume ratio than in patients who were in the compensated stage .

Xiao-li Chen and colleagues conducted a study employing MRI in 2014 for the purpose of quantitative evaluation of the severity o f cirrhosis in hepatitis B patients utilizing spleen size and right liver lobe volume. The study reveals

- decreasing RV with rising Child-Pugh score
- increasing SV with increasing Child-Pugh score
- significant correlation between decreasing RV/SV ratio and increasing Child-Pugh score.(2)

Our analysis revealed that the right lobe liver volume decreases with increasing or worsening CTP (Child-Turcotte-Pugh) scores.

During decompensation, there is a discernible decrease in the volume of the liver, in especially the right lobe. The pathophysiology is connected to the perfusion of the portal vein. As fibrosis progresses and regeneration nodules grow, the pressure in the intrahepatic portal vein rises, and as a direct result, the amount of blood that flows to the liver decreases. (2)

According to the findings of our research, the CTP scores exhibits a pattern of correlation with RV/SV. This is because individuals with liver cirrhosis typically demonstrate splenic enlargement and shrinkage of liver especially the right lobe.

Yosuke et al. in the year 2008, carried out a study in Japan to determine the prognosis of primary biliary cirrhosis based on the volume ratio of liver to spleen.

They reached the conclusion that among the patients with primary biliary cirrhosis the percentage of patients who had symptoms were in the group with a low LV/SV ratio. (7)

Liu et al, in 2009 assessed variations in liver and spleen volume in patients with hepatic fibrosis.

Both the LV/SV ratio and the SLV/SV (standard liver volume to spleen volume**)** ratio had a steady and statistically significant drop as the degree of the fibrosis increased. (8)

Due to relatively less number of patients with NASH (Non alcoholic steatohepatitis) and viral etiology in our investigation, cirrhosis patients were broadly divided into two groups: alcoholic and non alcoholic.

Patel et al., in their research found that the patients diagnosed with NASH were shown to have a considerably greater spleen size and a lower ratio of liver to spleen when compared to individuals diagnosed with alcoholic and viral etiologies.(6)

Despite the fact that specific volume reduction exist depending on the etiology, due to a lack of sufficient samples in viral and NASH etiology that was not categorised. However in general, there was reduction in right lobe volume of liver for all etiologies.

Limitations Of CTP and MELD Score

Hepatic encephalopathy and ascites are just two of the disadvantages or limitations related to the use of the CTP score. These characteristics are open to interpretation and may be impacted by medical therapy.(9)
Employing the MELD score has certain inherent limitations in a similar way.

- Due to the fact that multiple laboratories employ varied techniques, the serum creatinine value can change from one laboratory to another.
- The findings of INR calculations performed at several locations using a number of different assays varied for each facility.
- In order to standardize the anticoagulant impact of warfarin, the international normalized ratio (INR) was created, although it may not adequately reflect the severity of liver disease.

Limitations

- Because clinical parameters are changing in conjunction with decompensation, it is possible for there to be a disparity between volumetric parameters and clinical grading at any one point in time.

- Clinical grading of cirrhosis is straightforward and requires less time, whereas volumetry is laborious, requires specialized software, and takes significantly more time.
- Since the majority of CT scans in chronic liver diseases are performed only in the later stages of the disease, early volume changes were not able to be identified in the majority of patients.
- In contrast to other etiologies, the volume of spleen and liver alterations in NASH act differently. Since there were fewer NASH cases in our study, there was no impact on the volume alterations in the liver and spleen.

CONCLUSION

- It is possible to employ non-invasive volumetric parameters like as RV,SV,RV/SV, and SI as useful indicators for determining severity of cirrhosis using MDCT.
- With increasing Child status of cirrhosis, RV/SV and RV tend to decline (p=0.001 and p=0.004, respectively), while SV tends to rise (p=0.005).
- RV/SV was the best noninvasive factor for distinguishing liver cirrhosis between Child-Pugh classes A and B (AUC = 0,706), A and C (AUC = 0.795), and B and C (AUC=0.644) among these volumetric measurements.

Clinical Application

MELD score is taken as a criteria for patient selection in TIPSS procedure. In some scenarios where elevated MELD score due to raised creatinine is hindering the patient from taking up for TIPSS, volumetry can help in predicting the actual liver status. Elevated creatinine can be managed by dialysis and the correction of other parameters would qualify the patient for procedure.

REFERENCES

(1) Tsochatzis, E. A., Bosch, J., & Burroughs, A. K. (2014). Liver cirrhosis. *Lancet (London, England)*, *383*(9930), 1749–1761. https://doi.org/10.1016/S0140-6736(14)60121-5

(2) Chen, X.-L., Chen, T.-W., Zhang, X.-M., Li, Z.-L., Zeng, N.-L., Li, T., Wang, D., Li, J., Fang, Z.-J., Li, H., Chen, J., Liu, J., Xu, G.-H., Ren, J., Wu, J.-L., & Li, C.-P. (2014). Quantitative assessment of the presence and severity of cirrhosis in patients with hepatitis B using right liver lobe volume and spleen size measured at magnetic resonance imaging. *PloS One*, *9*(3), e89973. https://doi.org/10.1371/journal.pone.0089973

(3) Tong, C., Xu, X., Liu, C., Zhang, T., & Qu, K. (2012). Assessment of liver volume variation to evaluate liver function. *Frontiers of Medicine*, *6*(4), 421–427. https://doi.org/10.1007/s11684-012-0223-5

(4) Saygili, O. B., Tarhan, N. C., Yildirim, T., Serin, E., Ozer, B., & Agildere, A. M. (2005). Value of computed tomography and magnetic resonance imaging for assessing severity of liver cirrhosis secondary to viral hepatitis. *European Journal of Radiology*, *54*(3), 400–407. https://doi.org/10.1016/j.ejrad.2004.08.001

(5) Yamagishi, Y., Saito, H., Tada, S., Horie, Y., Kato, S., Ishii, H., Shimojima, N., Haga, J., Shimazu, M., Kitajima, M., & Hibi, T. (2005). Value of computed tomography-derived estimated liver volume/standard liver volume ratio for predicting the prognosis of adult fulminant hepatic failure in Japan. *Journal of Gastroenterology and Hepatology*, *20*(12), 1843–1849. https://doi.org/10.1111/j.1440-1746.2005.03949.x

(6) Patel, M., Tann, M., & Liangpunsakul, S. (2021). CT-scan Based Liver and Spleen Volume Measurement as a Prognostic Indicator for Patients with Cirrhosis. *The American Journal of the Medical Sciences*, *362*(3), 252–259. https://doi.org/10.1016/j.amjms.2020.10.031

(7) Murata, Y., Abe, M., Hiasa, Y., Azemoto, N., Kumagi, T., Furukawa, S., Matsuura, B., Michitaka, K., Horiike, N., & Onji, M. (2008). Liver/spleen volume ratio as a predictor of prognosis in primary biliary cirrhosis. *Journal of Gastroenterology*, *43*(8), 632–636. https://doi.org/10.1007/s00535-008-2202-9

(8) Liu, P., Li, P., He, W., & Zhao, L.-Q. (2009). Liver and spleen volume variations in patients with hepatic fibrosis. *World Journal of Gastroenterology*, *15*(26), 3298–3302. https://doi.org/10.3748/wjg.15.3298

(9) Gotthardt, D., Weiss, K. H., Baumgärtner, M., Zahn, A., Stremmel, W., Schmidt, J., Bruckner, T., & Sauer, P. (2009). Limitations of the MELD score in predicting mortality or need for removal from waiting list in patients awaiting liver transplantation. *BMC Gastroenterology*, *9*, 72. https://doi.org/10.1186/1471-230X-9-72