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ORIGINAL ARTICLE

Donor Liver Attenuation Index and Liver Biopsy Correlation in Living Donor Liver Transplantation

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ABSTRACT

Objective: Using non-invasive methods, such as BMI and CT LAIto suggest a prediction model for hepatic steatosis, examine the CT liver attenuation index and body mass index (BMI)association for pathological steatosis in living liver donors. Histological analysis remains the standard reference.

Study Design: Retrospective study

Place and Duration of Study: Liver Transplantation Department, Bahria International Hospital Orchard, Lahore from 1st June 2017 to 31st December 2018.

Methodology: Fifty-nine donors were included with a median age of 23.00 years, as well as the potential donors for LDLT who experienced evaluation as a potential liver donor. Donors who underwent CT scan and histological liver evaluation were part of this study.

Results: Of the donors, forty-eight **(**81.35%) had a CT LAI ≥1. The median BMI was 22.1 (range: 17.00–33.4). Twenty eight (47.5%) of the patients had undergone liver biopsy for screening in the pre-transplant period whereas 31 (52.5%) of the total evaluated donors underwent biopsy during the transplant. Thirty four (57.62%) out of 59 evaluated living liver donors underwent hepatectomy. Non-significant association (P=0.719) between different categories of BMI as the steatosis increases histologically, whereas significant association (P<.05) for CT LAI as the steatosis increases histologically.

Conclusion: Body mass index alone is not a reliable factor for liver fat estimation non-enhanced CT liver-spleen attenuation index of ≤0 correspond to severe hepatic steatosis reserving histopathological liver evaluation via biopsy for selected cases and decreasing the need of liver biopsy while making sure both donor and recipient are safe.

Keywords: Living donor liver transplantation, CT LAI, BMI, Liver biopsy

INTRODUCTION

The valuation of hepatic steatosis is crucial for the selection of a living liver donor, because most of the healthy individuals are declined to be a liver donor if hepatic steatosis is found significant in liver parenchyma.[1] As it can have an effect on the postoperative outcomes in the donor and can lead to serious complication as donor liver dysfunction.In addition, recipients with fatty grafts are at risk of loss of function at early stage post-transplant, poor overall graft survival,primary dysfunction, and other difficulties.[2,3]Therefore, pre-operative hepatic steatosis assessment is pivotal to good donor and recipient outcome.[1]

Despite various biochemical, anthropometric, and radiological methods beingthouroughly assessed, donor liver biopsy still remains the benchmark for quantification of liver parenchymal steatosis.[4-7]However,biopsy's invasiveness, cost, possibility of sampling error, potential risk of hemorrhage, and intra- and inter-observer variability during pathological interpretation make it unsuitable as a screening investigation.[4]

Several noninvasive imaging modalities have been suggested to examine liver donors for steatosis, including ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). Computed tomography being a less invasive and reliable mode of assessing ≥30% macrovesicular steatosis has been considered as an initial assessment investigation which might decrease the need for liver biopsy in living donors.[4,6-8] Body mass index is another tool for quantifying moderate degree of steatosis with cut-off values of >23 and >27.5 for different population groups. But no such data exists for living donors which is country-specific or ethnic-specific for south Asians.[8,9]

MATERIALS AND METHODS

This retrospective study was conducted at Liver Transplantation and Hepato-Pancreatico-Biliary Surgery Department of Bahria International Hospital Orchard, Lahore from 1st June 2017 to 31st December 2018. The potential donors for LDLT who experienced evaluation as a potential liver donor inDonors who underwent CT scan and Liver biopsy were included in this study. Informed written consent was taken from all donors for every procedure and to use their data for study purpose. The process of evaluation started after a brief meeting with senior transplant surgeon in his clinic and establishing volunteer process of donation. Initial screening of donors with blood grouping, complete blood count, liver function tests, renal function tests, coagulation profile and hepatitis profile was done. The presence of Hepatitis B antigen, anti HCV antibody and antibodies to HIV marked exclusion of that donor at this step.

Blood related donors without any known illness, from 18 to 50years of age, with a compatible blood group are considered optimal donors. Abdominal ultrasonography was done on all optimal donors to evaluate liver parenchymal quality including hepatic fatty change and liver Doppler. Triphasic contrast-enhanced C.T scan was done to evaluate anatomy of donor liver and also used to calculate volumes of liver to ensure adequate graft size for recipient and sufficient remnant volume in the liver for the donor after hepatectomy. Graft recipient weight ratio (GRWR) and future liver remnant (FLR) approximations were made using available live volumes. Cut off for GRWR was 0.8 and for FLR was 30%. Any donor having GRWR and FLR less than this value was not further evaluated. Without contrast CT used for LAI calculation in all patients, those who had LAI from 5 to 15 underwent further evaluation procedure. LAI less than -10 Hounsfield units (HU) was a cutoff value and liver donation was not considered in all such donors. Liver biopsy is taken into consideration in all donors having LAI between 5 and -10 HU. Proposed donors with abnormal liver function tests, donors with BMI greater than 27 who are losing weight and willing for donation, blood relative of a person with autoimmune or genetic liver disorder are subjected for liver biopsy. Donors that showed signs of sever fatty change, unfavourable hepatic parenchyma, and complex liver anatomy, not amendable for safe resection, were excluded. Later on MRCP was done to delineate biliary anatomy once suitability of donor has been assessed.

Non-enhanced and enhanced CT scan with multi-detector row helical scanner was done on all donors to detect any abnormal lesion and to assess vascular anatomy. Volumetric assessment of liver was performed by Itellispace Portal Radiology DICOM image processing application software version 8 (CT ingenuity 128 slice Philips Cleveland, USA).On every scan 2 areas of interest from every segment of liver were acquired. Liver and spleen densities in Hounsfield units (HU) were taken and used to calculate liver to spleen attenuation difference to analyze hepatic steatosis. Liver attenuation was taken by calculating average of HU of two 1 to 1 cm^2 regions of interest in every segment. Three to four random attenuations were taken from different splenic levels on axial images to calculate average splenic attenuation.

Liver sample were taken from all donors for histological assessment of steatosis. Non-selective Core biopsies were taken from right lobe of liver under ultrasound guidance where indicated. Rest of the donors underwent wedge resection from segment 4 during transplant surgery. All biopsy samples were analyzed by single transplant pathologist who was not aware of findings of radiological images and grading of steatosis was done in percentages.

The data was inspected by using SPSS version 20. Fisher's exact or chi-square test was applied on categorical variables. Pearson correlation test was applied between different variables to demonstrate their relation. The value of P=<0.05 was considered significant.

RESULTS

The group was composed of 44 males (74.6%) and 15 females (25.4%). The median age was 23 years (range: 18–49 years). None of the patients suffered from hypertension or diabetes. The liver attenuation index of potential liver donor ranges from −16.00 to 19.9. Candidates having CT LAI ≥1 were 81.35% (48). The median BMI was 22.1 (range: 17.00–33.4). 17 (28.81%) donors fall inthe overweight category because of their increased BMI (25–29.9 kg/m^2). 28(47.5%) of the patients underwent liver biopsy for screening in the pre-transplant period whereas 31 (52.5%) of the total evaluated donors underwent biopsy during the transplant.Additionally, 3 (5.1%) of the 59 donors had more than 30% steatosis on histology (Fig. 1). The number of patients with greater than 5% and less than 15% hepatic steatosis were 2 (3.4%). Accordingly 34 (57.62%) out of 59 evaluated living liver donors underwent hepatectomy.For the donor operations, alldonorsunderwent right hepatectomy.

Parametric analysis for BMI and liver biopsy showed weak positive correlation (r =0.25). Chi-square test yielded non-significant association (P=0.719) between different categories of BMI (less than 18, 18.1-24.9, 25-29.9 and more than 30) as the steatosis increases histologically (no steatosis,0–5, 6-15, 15–30, >30). The Chi-square test showed significant association (P<.05) for categories of CT LAI (<0, 0–5 and 6-15, >15) as the steatosis increases histologically.

Non-parametric analysis of CT LAI and liver biopsy steatosis showed negative correlation significantly with correlation coefficient of -0.58 as depicted in figure 02. .3 donors among all had ≥30% fatty change in liver parenchyma on biopsy. In 3 of 3 donors C.T LAI was less than -5 showing that CT derived steatosis prediction was 100% correct for donors having high steatosis on biopsy.

Mild degree of peri-portal inflammation along with cholestasis was evident in 8 out of 59 donors on histology without any significant steatosis. These patients did not have significance steatosis on liver attenuation indices. These mild changes were also occult on radiological imaging including ultrasound and contrast enhanced CT scan.

Table 1: Distribution of donors with respect of CT LAI and steatosis grading (n=59)

CT LAI	No. steatosis	Histopathological grading		
		< 5%	5 - 15%	>30%
<0	6	1	1	3
0-5	9	2	0	0
6-15	29	3	1	0
>15	4	0	0	0

Table 2: Distribution of donors with respect of CT LAI and BMI (n=59)

CT LAI	Body mass index (kg/m^2)			
	<18	18.1-24.9	25-29.9	>30
<0	0	4	4	3
0-5	1	5	5	0
6-15	3	25	4	1
>15	0	3	1	0

Table 3: Distribution of donors with respect of histopathological grading and BMI (n=59)

BMI (kg/m^2)	No. steatosis	Histopathological grading		
		< 5%	5 - 15%	>30%
<18	4	0	0	0
18.1-24.9	31	4	1	1
25 -29.9	10	2	1	1
>30	3	0	0	1

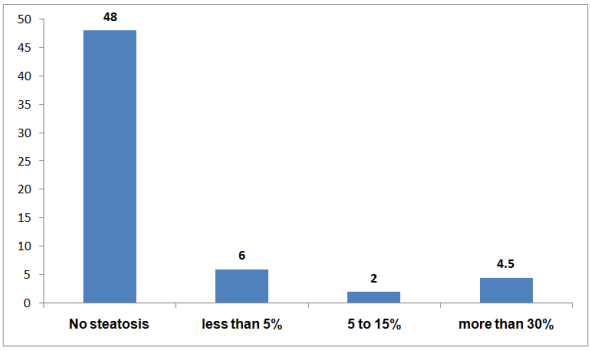

Fig. 1: Frequency of donors with steatosis

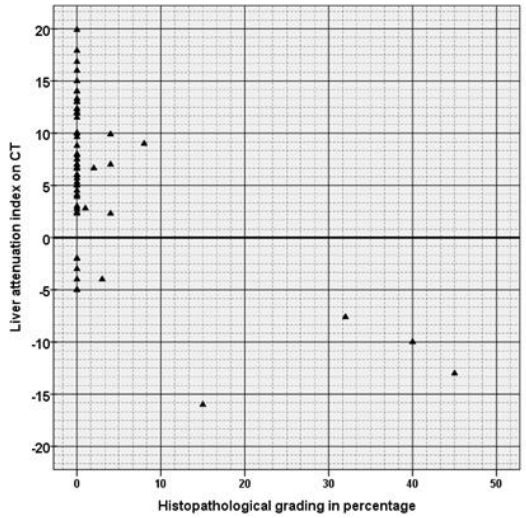

Fig. 2: Scatter plot of LAI and steatosis

DISCUSSION

It is essential to preserve donor health and exclude unfavorable candidates when considering donations as healthy volunteers can donate a partial liver graft to the respective compatible patient. Risk to the healthy donor has always been a matter of serious ethical concern for LDLT. Liver parenchymal fatty infiltration is one of the main reasons that precludes a healthy individual from being a liver donor Thus, an accurate quantitative analysis of liver parenchymal fat in donors is vital for the proper selection of liver grafts.

Fatty infiltration in liver presents in a variable range from uniform steatosis to heterogeneous distribution, right lobe of liver being more affected as it gets major contribution of vascular supply from the portal circulation.[10]

Histological evaluation through liver biopsy is the standard diagnostic reference investigation for assessment of liver parenchymal fatty infiltration and its quantification. Liver biopsy is an insight to fat distribution in different lobes of liver i.e. steatosis. Steatosis is of two major types, micro- and macrovesicular patterns, depending on the distribution and size of fat vacuoles in hepatocytes cytoplasm. Invasiveness being the most pronounced Limitation to histological examination, other sampling errors in patients subjective to heterogeneous pattern of hepatic steatosis.[11] A reported 20% incidence of pain after liver biopsy makes it an unpleasant experience to donors as well.

Different CT scan techniques have been used for liver parenchymal fatty infiltration, but non-enhanced CT scans are found to be best among all. It avoids the possible errors of contrast-enhanced variations in liver attenuation related to contrast injection methods and scan timing. There have also been several studies confirming this method to be highly sensitive (88%-95%), and accurate (90%-99%) for detecting hepatic steatosis. [1,12]

In the present study, difference in LAI values of liver and spleen was evaluated. In our subject group 33 donors had LAI between 6 to 15 which corresponded with minimal to no steatosis (0 to 15%), the eleven donors showed considerable fatty infiltration on histopathology and with CT LAI being ≤0. Among these 11 donors, 4 (36.36%) had moderate to severe fatty liver whereas, 3 donors (27.27%) had ≥30% hepatic fat infiltration on histopathology which was accurately predicted by a CT LAI of ≤0 in all 3 cases. The results of our study in detecting moderate to severe steatosis on CT LAI is comparable to the previous reported studies.[4,13] From our study results we can propose that candidate who underwent liver donor evaluation and turn out to have moderate to severe liver parenchymal fat infiltration on CT imaging should not undergo liver biopsy so that associated risks can be avoided and will be cost effective, whereas CT scan can be used to clinically evaluate which living liver donors should be declined based on liver parenchymal fat being >10%.

Body mass index has always been considered as an individualistic factor for liver parenchymal fat prediction. BMI values vary among different population groups in predicting degree of liver steatosis.[9,14,15] This study showed that found no correlationbetween liver biopsy and BMI. Fourteen donors (23.7%) of our study population were overweight whereas only one had significant steatosis. So, it seems to biological to accept overweight donors for evaluation and every individual donor should be evaluated clinically and BMI evaluation should be done accordingly.[15,16]

The limitations of our study were of relatively small data with selected candidates as most of the donors included were of normal BMI and probable liver donors with suspicion of severe steatosis were not a part of initial donor evaluation, and only 3 patients with severe steatosis were included. Although being a retrospective study, there were no missing data.

CONCLUSION

Histopathological evaluation is standard for liver parenchymal fat infiltration. In our study population, BMI alone is not a reliable factor for liver fat estimation. Non-enhanced CT liver-spleen attenuation index of ≤0 correspond to severe hepatic steatosis and CT LAI of >6 also correspond with slight degree of hepatic steatosis in living liver donor candidates, thus reserving liver biopsy for selected cases and decreasing the need of liver biopsy while making sure donor and recipient are safe.

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