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Original Article

Effects of fatty filtration at the pediatric liver hemodynamic changes evaluated by Doppler ultrasonography

Çocukluk dönemi karaciğer yağlanmasındaki hemodinamik değişikliklerin Doppler sonografi ile değerlendirilmesi

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ABSTRACT

Background: Hemodynamic changes in liver vascular structures of patients in the pediatric age group are evaluated by doppler ultrasonography.

Material: Fifty- nine hepatosteatosis patients, classified as mild, moderate or severe, and 23 healthy volunteers were included in this 82-person study. The height, weight, liver size tests of the subjects were measured. Those values were compared in the patient and control groups. In the patient and control groups, color duplex Doppler ultrasonography was used to examine portal vein peak velocity, portal vein flow volume, hepatic artery resistive index (RI), hepatic artery pulsatility index (PI) and hepatic artery flow volume.

Results: Similar to the degree of hepatosteatosis, increases in body mass index, liver size were statistically significant ($p<0.05$). The difference between portal vein peak velocity hepatosteatosis and control groups was found statistically significant. As the hepatosteatosis grade increased, there was no statistically significant decrease in hepatic arterial flow volume, portal vein flow volume, and total flow volume. Hepatic artery RI and PI values were statistically significantly lower in the control group than the other groups ($p <0.05$). There was a significant mild decrease in the mild stool group compared to the middle steat group. Although the hepatic artery RI and PI values did not differ statistically in the comparison of the hepatosteatosis group, there was a minimal increase in the RI and PI values as the steatosis grade increased.

Discussion: According to these results, as the level of steatosis increases, the changes in the portal venous structures become more prominent and the resistance increases in vascular structures.

Keywords: Doppler sonography, pediatric fatty liver

ÖZ

Giriş: Pediatrik yaş grubundaki hastaların karaciğer vasküler yapılarındaki hemodinamik değişikliklerin doppler ultrasonografi ile değerlendirilmesidir.

Materyal / Metot: Bu 82 kişilik çalışmada, hafif, orta veya şiddetli olarak sınıflandırılan 57 hepatosteatoz hastası ve 23 sağlıklı gönüllü çalışmaya dahil edildi. Deneklerin boy, kilo, karaciğer büyüklüğü testleri ölçüldü. Bu değerler hasta ve kontrol gruplarında karşılaştırıldı. Hasta ve kontrol gruplarında portal ven tepe hızını, portal ven akım hacmini, hepatik arter rezistif indeksi (Rİ), hepatik arter pulsatilite indeksini (PI) ve hepatik arter akım hacmini incelemek için renkli dupleks Doppler ultrasonografi kullanıldı.

Sonuçlar: Hepatosteatoz derecesine benzer şekilde, vücut kitle indeksindeki artışlar, karaciğer boyutu,istatistiksel olarak anlamlıydı (p<0,05). Portal ven tepe hızii hepatosteatoz ve kontrol grupların arasındaki fark istatistiksel olarak anlamlı bulunmuştur. Hepatosteatoz derecesi arttıkça hepatik arter akım hacminde, portal ven akım hacminde ve toplam akış hacminde istatistiksel olarak anlamlı bir azalma görülmemiştir. Hepatik arter RI ve PI değerleri kontrol grubunda diğer gruplara göre istatistiksel olarak anlamlı derecede düşüktü (p <0.05). Hafif şteatoz grubunda, orta steatoz grubuna göre anlamlı hafif oranda düşüklük vardı. Hepatosteatoz grubunun kendi içinde karşılaştırılmasında, hepatik arter RI ve PI değerleri istatistiksel olarak farklılık göstermese de steatos derecesi arttıkça RI ve PI değerlerinde minimal bir artış vardı.

Tartışma: Bu sonuçlara göre steatos derecesi arttıkça portal venöz yapılardaki değişiklikler daha ön planda olmakla birlikte vasküler yapılarda direnç artışı da meydana gelmektedir.

Anahtar kelimeler: Doppler sonografi, pediatrik dönem, yağlı karaciğer

INTRODUCTION

Hepatosteatosis is the accumulation of excess fat in the liver by more than 5%. Early stage steatosis does not cause serious problems, but cirrhosis can lead to progressive stages. In the pediatric age group, the causes of steatosis vary in a wide spectrum including metabolic diseases, non-alcoholic fatty liver diseases and obesity [1–6]. Although steatosis is considered reversible, it must be confirmed by biopsy depending on the effect. Because USG is non-invasive, cheap and reproducible, it is the preferred diagnostic method for the diagnosis of steatosis in the pediatric age group [4,5].

Sonoelastography, which provides measurement of tissue stiffness, increases the diagnosis and progression of steatosis, and limits the value of early stage diagnosis in diseases such as NAFLD [7]. It has now led to the necessity of understanding the pathology of steatosis with the cause of increased incidence of obesity [7,8].

In the adult age group, studies to explain the changes in the liver vascular bed have been made, but the effects on the childhood age group are limited [1,9].

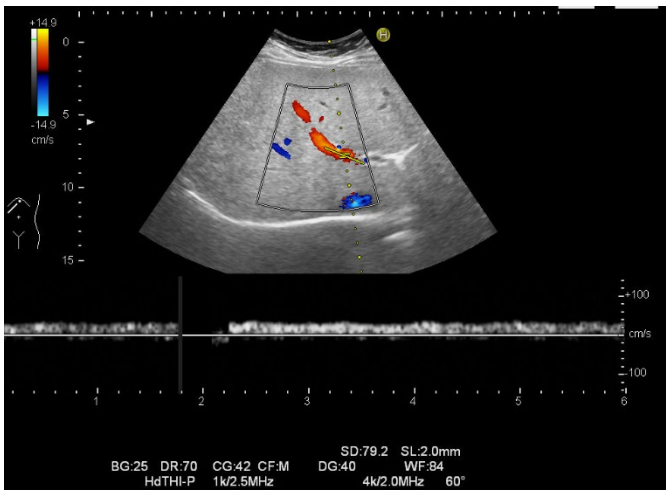
The aim of this study is to understand the physiopathology of vascular inpatients using the Doppler USG technique in the comparison of different stages of steatosis in the pediatric age group.

MATERIALS AND METHODS

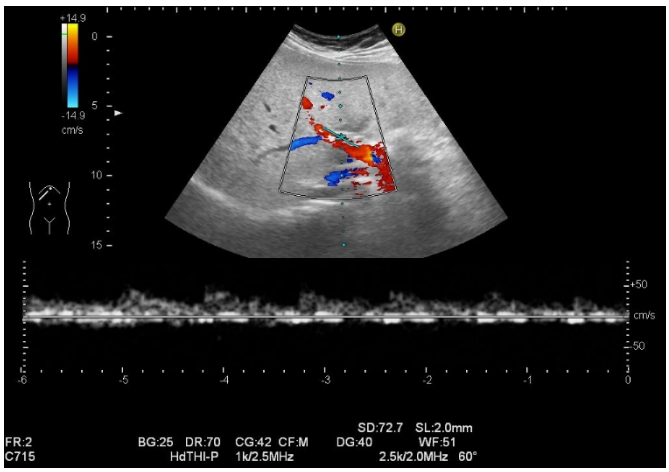
Patients who were referred to the pediatric gastroenterology polyclinic for obesity were evaluated retrospectively. The control group consisted of patients who were referred to the same polyclinic with dispeptic complaints. Doppler examinations were performed for ultrasonography and hepatic arterial in the outpatient clinic, and patients enrolled in our imaging radiology records were included in the study.

The presence of any person other than obesity from the etiologic factors that may be caused by hepatosteatosis was considered as the criterion for exclusion. The cases in the control group consisted of healthy individuals who had no known systemic problems and only dispeptic complaints. According to age and gin, body mass index was 95 percent greater than that of obese.

Routine sonographic evaluation was performed in a quiet room, supine position, subcostal or intercostal approach after at least 8 hours of fasting. Doppler spectral recordings were performed at 30-60 degrees using sampling interval of 1/2 -1/3 of artery diameter at the time of breath holding after inspiration. The study used records of the main hepatic



(a)



(b)

Figure 1. A thirteen years old boy with a slightly fat infiltrated liver underwent sonography examination. (a) Doppler examination shows monophasic waveform at portal vein. (b) The hepatic artery with the appropriate patient position and angle sonation, the waveform obtained by doppler sonography

artery Doppler parameters at portal hilus level and records of current volume and liver parenchyma echogenicity. Patients were informed about the application in our department.

Patients in the supine position were examined from subcostal or intercostal approaches. On the midclavicular line in the sagital plane, the craniocaudal size of the liver was measured. After hepatosteatosis diagnosis was confirmed, the degree of hepatosteatosis was classified as mild (grade I), moderate (grade II) or severe (grade III) using USG data.

Patients with a slight increase in the diffusion of liver echogenicity, with normal echogenicity of the diaphragm and intrahepatic vein walls were classified as grade I hepatosteatosis. Increased liver echogenicity, with minimal washout of intrahepatic vein walls and diaphragm echogenicity were evaluated as grade II hepatosteatosis. Patients with a definite increase in liver echogenicity with posterior segments of the liver not clearly visible and intrahepatic vein walls and diaphragm partly or fully obscured were classified as grade III hepatosteatosis.

After hepatosteatosis investigation was completed, portal vein and hepatic artery were examined using color duplex Doppler. Patients were examined in supine or left lateral decubitus position. A 3.5 MHz convex probe was used. Vascular structures were investigated with gray scale, color Doppler and spectral Doppler USG (**Figure 1a**, **1b**).

Portal vein between splenoportal junction and intrahepatic bifurcation was visualised as an anechoic tubular structure on gray-scale images. On color Doppler, the lumen was fully filled with homogeneous color and flow direction was towards the liver. On spectral exam the sample window was located in the center of the lumen. The flow cursor was placed parallel to the portal flow. While the portal flow was examined, the angle was held between 30–60 degrees. For that reason, the majority of patients were examined in the left lateral decubitus position. As portal vein flow reflects the respiratory phase, flow measurements were made while the patients held their breath.

After the patient inhaled and held their breath, the flow spectrum was examined and images were frozen to measure and record portal vein diameter, velocity, and flow volume.

The hepatic artery was examined by Doppler USG after deep inspiration, in right intercostal or subcostal direction. The diameter of the hepatic artery is much smaller than of the portal vein and due to anatomic variations, it was difficult to observe in some patients. The majority of examinations showed the hepatic artery anterior and slightly diagonal to the portal vein on a 30–60-degree angled image. On spectral examination, at least three consecutive wave forms were used to measure hepatic artery diameter, peak systolic speed, end diastolic speed, RI, PI, and flow volume.

After USG examination was complete, the patients' height and weight were measured and body mass index (BMI) was calculated.

StatPlus V6 were used as the statical analysis program. Continuous variables were given as mean, standard deviation, minimum and maximum values; categorical variables were given as frequency and percentages. Normal distribution of variables was tested with the Shapiro-Wilk test. Comparison of normally distributed variables in 3 or more groups was completed with one-way analysis of variance (ANOVA). Paired comparisons used the post-hoc test. Variables not compliant with parametric tests were compared using the Mann-Whitney U test for paired

Table 1. Mean liver size, BMI and portal vein peak velocity values according to groups and relevant p values

Variables	Group 1 (control group)	Group 2 (Grade I hepatosteatosis)	Group 3 (grade II hepatosteatosis)	Group 4 (Grade III hepatosteatosis)	p value
Liver size	127.31	149.66	157.79	181.625	0.001
BMI	19.7	25.6	31.9	34.2	0.01
Portal vein peak velocity	33.6	39.8	42.1	38.1	0.023

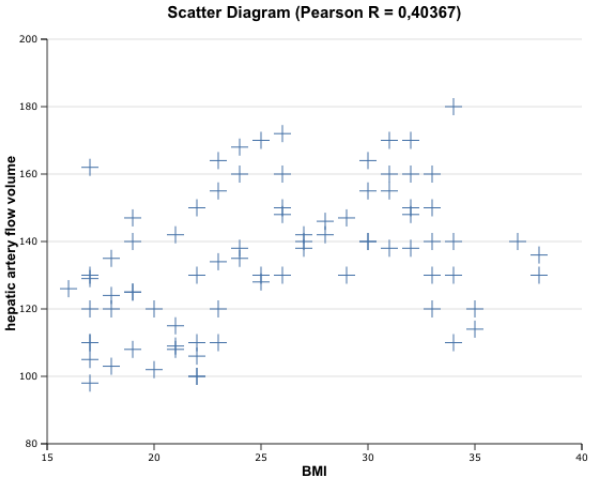


Figure 2. The scatter diagram analysis of correlation between body mass index and hepatic artery flow volume (r=0.403)

comparisons and Kruskal Wallis test for 3 or more group comparisons. Relationships between continuous variables were interpreted using the Spearman correlation coefficient. A p value of less than 0.05 was accepted as significant.

RESULTS

A total of 82 cases were evaluated. The control group of 23 healthy people without hepatosteatosis, and other groups of mild 28 patients (grade I), 23 patients moderate (grade II) and 8 patients severe (grade III) hepatosteatosis, were analysed. The control group comprised 9 males and 14 females between the age of 7 and 18; grade I hepatosteatosis group included 16 males and 12 females between the age of 6 and 17; grade II hepatosteatosis group included 11 males and 12 females between the age of 7 and 18 while the grade III hepatosteatosis group included 5 males and 3 females between the age of 9 and 17.

Liver size, Body Mass Index values for each group were detailed in (**Table 1**). When the groups were compared with each other, statistically significant differences were found (p=0.001). In the correlation analysis, liver size and BMI were positively correlated with hepatosteatosis (r=0.629). In

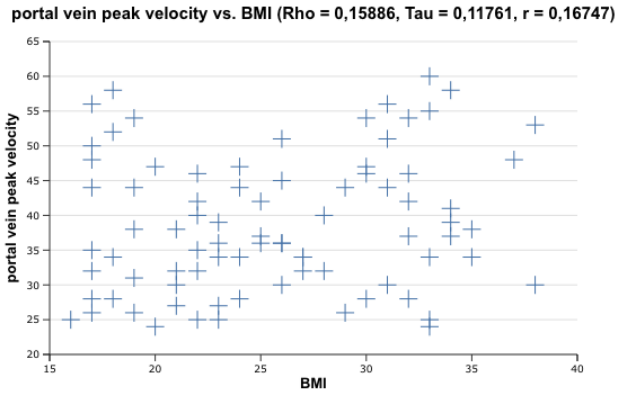


Figure 3. The scatter diagram analysis of portal vein peak velocity and body mass index (r=0.167)

Table 2. Doppler ultrasonographic parameters according to groups and relevant p values

Variables	Group 1 (Control group)	Group 2 (Grade I hepatosteatosis)	Group 3 (Grade II hepatosteatosis)	Group 4 (Grade III hepatosteatosis)	*p* value
Portal vein flow volume	719.36	671.07	729.16	648.75	0.273
Hepatic artery flow volume	123.67	135.48	145.20	136.20	0.53
Hepatic perfusion index	0.782	0.812	0.761	0.734	0.631
Hepatic artery RI	0.61	0.66	0.698	0.696	0.021
Hepatic artery PI	1.022	1.266	1.24	1.325	0.038

RI – resistivity index; PI – pulsatility index. Data were given as mean ± standard deviation.

Figure 2, the body mass index and the hepatic artery flow correlation analysis were mentioned.

While portal vein peak velocity measured on Doppler USG was not significant between the groups, there was a decrease with increase in the degree of hepatosteatosis (p=0.207) (**Table 1**). In **Figure 3** the portal vein peak velocity and the BMI correlation is shown.

Between the groups there were no significant statistical differences in hepatic artery flow volume (p=0.53), portal vein flow volume (p=0.273), hepatic perfusion index (p=0.631). Between the groups there was a statistically significant difference in hepatic artery RI (p=0.021) and hepatic artery PI (p=0.038) (**Table 2**).

When we compared hepatic artery (HA) RI and PI values in patient group and control group; we observed increase that is statistically significant. This significant changes include Comparing HA RI and PI values in Group 2 (grade I hepatosteatosis), Group 3 (grade II hepatosteatosis) and

Table 3. Mean hepatic artery RI and PI values according to groups and relevant p values for double-group comparisons

	Hepatic artery RI	p value	Hepatic artery PI	p value
Group 1 **Group 2**	0.61 0.66	0.001	1.022 1.266	0.001
Group 1 **Group 3**	0.61 0.698	0.001	1.022 1.24	0.001
Group 1 **Group 4**	0.61 0.696	0.001	1.022 1.32	0.001
Group 2 **Group 3**	0.66 0.698	0.01	1.266 1.24	0.948
Group 2 **Group 4**	0.66 0.696	0.069	1.266 1.32	0.815
Group 3 **Group 4**	**0.698** **0.696**	**0.99**	**1.241** **1.32**	**0.604**

Group 4 (grade III hepatosteatosis) with Group 1 (control). To identify paired groups in regards of hepatosteatosis where HA RI and PI values were significant, results indicated only a significant increase between Group 2 and Group 3 HA RI values (p=0.01). There were not any other significant changes in terms of at the comparison of hepatic artery resistive and PI values at the patient group (**Table 3**).

DISCUSSION

Hepatosteatosis is an increasingly reversible public health problem in childhood that develops as a secondary to obesity [10,11]. The exact diagnosis is made histopathologically. With techniques such as USG and elastography, it can be diagnosed with high specificity and sensitivity [7]. In this study, it was aimed to investigate the changes in steatosis grade and vascular area in childhood patients with hepatosteatosis diagnosed using doppler USG.

In this study, 6 to 18 year old cases were examined. Four groups of normal (control) or mild, moderate and severe hepatosteatosis were formed and compared in 82 subjects. There was a statistically significant difference between the mean values when comparing the groups in terms of liver size and BMI. As hepatosteatosis grade increased, there was a significant increase in liver size and BMI. In addition, the correlation between BMI and liver size was statistically significant (r=0.629).

All the portal vein measurements in the study were obtained at the monophonic stage for getting appropriate results. When comparing the portal vein peak velocity between the control group and hepatosteatosis group, we found a statistically significant different but a slightly weak correlation linked to the degree of steatosis (p=0.023, r=0.167). However, within the comparison of steatosis groups there was not any statical difference has been found. In literature Ulusan et al. and, Karasin et al. found a significant decrease between the mean velocity and the hepatosteatosis group [1,12]. But these studies were done at the adult age groups. In our study group there were not such kind of a decrease within the steatosis group. The number of patients at the grade-3 steatosis group were only eight. Therefore, a large number of further studies should evaluate this issue.

There was no statistically significant difference (p> 0.05) between portal vein flow volume, hepatic arterial blood flow volume and hepatic perfusion index (hepatic arterial flow volume / total hepatic flow volume) between the control group and the patient groups. Portal vein and hepatic arterial flow volume were increased in the grade I and grade II hepatosteatosis groups without statistically significant increase. In the Grade III hepatosteatosis group, there is a statistically insignificant decrease when compared with the control group. Studies in the literature have concluded that as the hepatosteatosis grade increases, the flow volume decreases. As the fat density in the liver increases, the volumetric increase in hepatocyte volume may cause a pressure effect on the vasculature, leading to a decrease in flow volume.

Hepatosteatosis, portal vein, previously affects arterial structures and causes a decrease in portal venous flow and portal flow volume. The hepatic artery flow volume increases to compensate for this decrease. As the rate of fat ratio increases, the compensatory mechanisms stop and the arterial flow is affected, which causes a decrease in arterial flow, despite the decrease in portal volume. In hepatosteatosis, the hepatic perfusion index increases as the level of steatosis increases. When we compared hepatic perfusion index values between hepatosteatosis groups and hepatosteatosis groups in our study, no statistically significant difference was found (p>0.05). In our study, an increase in the hepatic perfusion index was observed only in the control group and

Steatosis was present in group 1 patients. There was a decrease in group 2 and 3 patients. However, none of these comparisons reached a statistically significant level (p>0.05). These findings support similar results when compared with studies in the adult group [1].

In our study, there was a significant difference between the control group and the steatosis groups between the hepatic artery PI and RI values. When compared with the control group, there is a significant difference between all steatosis groups. However, in the comparison of steatosis groups within themselves, only stage 1 steatosis was found to differ

between groups 2 and 3. There was no significant difference between groups 3 and 4. Hepatic artery RI values increased with control group and steatosis grade (r=0.697). This finding supports the findings of Hizli et al in the literature [13]. However, in the literature, Mihmanli et al. reported a correlation between elevated steatosis grade and decreased HA RI values [10]. They claimed that oil infiltration caused the compression of portal triad structures. This infiltration affected the portal vein earlier and caused a decrease in portal flow, leading to increased HA diastolic flow and decreased RI. Mohammadinia et al. Color Doppler and spectral Doppler USG were used to study HA RI in a study of 80 patients in the mild, moderate and severe hepatosteatosis group and in the control group [14]. There was a significant decrease in HA RI values with increasing hepatosteatosis grade.

In our study, there are incomplete aspects such as the inadequacy of grade 3 hepatosteatosis, the absence of any number of cases where parametric testing can be performed at every steatosis level and the absence of gold standart biopsy diagnosis showing the degree of steatosis. In addition, changes in the prepubertal and pubertal period in the volume of hepatic artery flow can be demonstrated by studies to be carried out in a wider series, and findings need to be supported by techniques such as elastography by decreasing dependency on the practitioner.

CONCLUSION

Hepatosteatosis causes changes in the vascular bed in the liver in childhood and these changes lead to increased resistance compared to the steatosis rate. Doppler USG is a useful method for understanding and monitoring hemodynamic changes.

DECLARATION OF CONFLICT OF INTEREST

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REFERENCES

1. Karasin M, Tokgoz O, Serifoglu İ, Oz İ, Erdem O. The doppler ultrasonographic evaluation of hemodynamic changes in hepatic vascular structures in patients with hepatosteatosis. Polish J Radiol. 2014.
2. Abdelmalek MF, Diehl AM. Nonalcoholic Fatty Liver Disease as a Complication of Insulin Resistance. Medical Clinics of North America. 2007; 91(6): 1125–1149.
3. Pico Aliaga SD, Muro Velilla D, Garcia-Marti G, Sanguesa Nebot C, Marti-Bonmati L. [Acoustic radiation force impulse imaging elastography is efficacious in detecting hepatic fibrosis in children]. Radiologia. 2015.
4. Alp H, Karaarslan S, Selver Eklioğlu B, Atabek ME, Altın H, Baysal T. Association be-tween nonalcoholic fatty liver disease and cardiovascular risk in obese children and adolescents. Can J Cardiol. 2013.
5. Uzun H, Yazici B, Erdogmus B, Kocabay K, Buyukkaya R, Buyukkaya A, et al. Doppler waveforms of the hepatic veins in children with diffuse fatty infiltration of the liver. Eur J Radiol. 2009.
6. Perito ER, Tsai PM, Hawley S, Lustig RH, Feldstein VA. Targeted hepatic sonography during clinic visits for detection of fatty liver in overweight children: A pilot study. J Ultra-sound Med. 2013.
7. Özkan MB, Bilgici MC, Eren E, Caltepe G, Yilmaz G, Kara C, et al. Role of Point Shear Wave Elastography in the Determination of the Severity of Fibrosis in Pediatric Liver Diseases With Pathologic Correlations. J Ultrasound Med [Internet]. 2017 Jun 6 [cited 2017 Aug 16]; Available from: http://doi.wiley.com/10.1002/jum.14277
8. Tuncel SA, Koçyiğit A, Demircioğlu F, Hızlı Ş. HC. Assessment of hepatic artery flow volume changes due to hepatosteatosis on pediatric obese patients. Pamukkale Med J. 2014; 7(2): 131–6.
9. Erdogmus B, Tamer A, Buyukkaya R, Yazici B, Buyukkaya A, Korkut E, et al. Portal vein hemodynamics in patients with non-alcoholic fatty liver disease. Tohoku J Exp Med. 2008.
10. Mihmanli I, Kantarci F, Yilmaz MH, Gurses B, Selcuk D, Ogut G, et al. Effect of diffuse fatty infiltration of the liver on hepatic artery resistance index. J Clin Ultrasound. 2005.
11. Tutar O, Beser OF, Adaletli I, Tunc N, Gulcu D, Kantarci F, et al. Shear wave elastography in the evaluation of liver fibrosis in children. J Pediatr Gastroenterol Nutr. 2014 Jun; 58(6): 750–5.
12. Ulusan S, Yakar T, Koc Z. Evaluation of portal venous velocity with doppler ultrasound in patients with nonalcoholic fatty liver disease. Korean J Radiol. 2011.
13. Hizli S, Kocyigit A, Arslan N, Tuncel SA, Demircioglu F, Cakmakci H, et al. Hepatic artery resistance in children with obesity and fatty liver. Indian J Pediatr. 2010.

14. Mohammadinia AR, Bakhtavar K, Ebrahimi-Daryani N, Habibollahi P, Keramati MR, Fereshtehnejad SM, et al. Correlation of hepatic vein doppler waveform and hepatic artery resistance index with the severity of nonalcoholic fatty liver disease. J Clin Ultrasound. 2010.

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