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Original Article

Correlation Between Portal Venous Dimensions and Liver Stiffness in Patients of Child Pugh A Cirrhosis

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Abstract

BackgrLiver cirrhosis is an end-stage liver disease characterized by pathologic fibrosis and regenerative nodules with resultant liver dysfunction. The diagnostic hallmark of portal hypertension is slow flow velocities in addition to the increased caliber of the mean portal vein. That is, the diagnosis of portal hypertension requires the measurement of mean portal velocity and portal diameter, and the correlation between cirrhosis and mean portal velocity and port diameter is the correlation between liver cirrhosis and its complications. The objectives of this study was to analyze the correlation between portal vein dimensions and liver stiffness in patients of Child-Pugh A cirrhosis.
Methods : This study was a cross-sectional study on 30 subjects with Child-Pugh A liver cirrhosis. The subjects of this research are patients who come to the Radiology Department of the Dr. Kariadi Hospital in Semarang for point shear wave elastography and abdominal ultrasound examination from January to December 2022. Spearman test correlation was used for the analysis.
Results : Spearman test showed no correlation between liver stiffness and portal vein diameter (p=0.250, r= -0.217), liver stiffness and mean portal vein velocity (p=0.883, r= -0.028), and portal vein diameter with mean venous velocity in Child-Pugh A liver cirrhosis (p = 0.979, r = 0.005).

Keywords : Liver stiffness, portal vein diameter, portal vein velocity, child-pugh A

INTRODUCTION

Liver fibrosis develops as a reversible consequence of a sustained or repeated wound-healing response to liver injury caused by viral, toxic, and/or metabolic insults, and represents an imbalance between the synthesis and degeneration of the extracellular matrix. Accompanied by the distortion of hepatic structure and function, cirrhosis is the result of the progression of liver fibrosis. Liver cirrhosis is a fatal condition with a high fatality rate. The 12th leading cause of death in the US and the fifth leading cause of death for adults between the ages of 45 and 54 is cirrhosis and its consequences. According to the latest Global Burden of Disease Study, the global incidence of cirrhosis and other chronic liver diseases in 2017 was 5,154,900.[3] Moreover, from 2007 to 2017, the years lived with disability (or 'YLDs') and all-age deaths from cirrhosis have increased by 34.8% and 15.0% respectively. Hence, the clinical burden of cirrhosis is substantial. Even so, the advancement of liver cirrhosis can be stopped or slowed down with prompt and accurate screening and diagnosis.[1,14,15]

Biopsy and histopathological evaluation remain the golden standard for assessing liver fibrosis. However, this procedure is painful and has many complications including bleeding (0.3%) and death (0.01%). Hence, early recognition of patients with chronic liver disease (CLD) at high risk for developing its complication in a noninvasive manner is warranted to allow the implementation of optimal preventative management strategies that may modify the natural course of the disease. Cirrhosis itself, on the other hand, causes stiffening, prompting standardized cut-off value for its measurement. Cirrhosis is also known to lead to portal hypertension and metabolic liver failure. Cirrhosis causes intrahepatic portal hypertension secondary to increased hepatic venular resistance caused by intrahepatic fibrosis. The diagnostic hallmark of portal hypertension is slow flow velocities in addition to the increased caliber of the mean portal vein. That is, the diagnosis of portal hypertension requires the measurement of mean portal velocity and portal diameter, and the correlation between cirrhosis and mean portal velocity and port diameter is the correlation between liver cirrhosis and its complications.[14–17,19]

The purpose of this study is to evaluate the relationship between liver stiffness in patients with Child-Pugh A cirrhosis and the dimensions of the portal vein. The findings of this study are anticipated to serve as a foundation for the management and predictors of mortality in liver cirrhosis.

METHODS

This study employs a cross-sectional methodology. The liver stiffness variable was measured using point SWE using Acuson S2000 from Siemens at RSUP Dr. Kariadi at a specific time throughout the research's data collection period, which ran from July 2022 to August 2022. The ethical council of the Faculty of Medicine at Diponegoro University, Semarang approved the procedure (No.1097/EC/KEPK-RSDK/2022). The cross-sectional study design was used to determine the sample size. In the study of Hong *et al*., the correlation coefficient between the diameters of the portal vein and the stiffness of the liver is 0.5. The minimal sample size is 30 subjects according to the sample size calculation.[5]

The inclusion criteria in this study are age ≥18 years old, Child-Pugh A classification of liver cirrhosis, clinical cirrhosis of the liver, previous sonography showing features of liver cirrhosis and not with acute chronic liver failure, history of iron overload, biliary obstruction (primary sclerosing cholangitis and cholestasis), and passive congestion leading to congestive hepatopathy (congestive heart failure, congenital heart disease with pulmonary stenosis and tricuspid regurgitation). The exclusion criteria for study subjects are invalid readings from point SWE or portal hypertension which is unlikely for technical reasons.[18]

The patient fasted for 4–6 hours before the examination. The examination was performed with the patient in a supine or left lateral position with the arm. The measurement was made through the intercostal space as the best location for the acoustic window. The transducer was then positioned perpendicular to the liver capsule about 1–2 cm below the liver capsule to avoid reverberation artifacts. The optimal measurement depth is 4–5 cm from the skin layer. Region of Interest (ROI) should avoid major vessels, bile ducts, costal/rib shadows, and masses. The ROI area is about 1 cm^3. The examination was carried out in a neutral position. The patient was asked to take a deep breath and hold it. The examination was repeated ten times. The median value of the examinations was then used as the result of the elastography examination. The diameter of the inner wall (lumen) of the portal vein was measured in millimeters using sonography. Doppler sonography was used to calculate the mean highest and lowest velocity of portal vein blood flow in centimeters per second.

To prove the relationship between portal vein dimensions and liver stiffness, the authors also collected data regarding the subjects' age, sex, BMI, duration of illness, history of previous illness, history of alcohol consumption, and the subjects' previous laboratory test results. The formula used to prove the correlation will be Pearson if the data distribution is normal, or Rank-Spearman if one or both of them are not normally distributed.

RESULTS

In this study, 30 patients already classified with the Child-Pugh classification were chosen; consisting of 17 men (56.67 %) and 13 women (43.33 %). Two-thirds of the subjects were more than fifty years old (66.67%). Twenty-six of the samples (86.67%) have been ill for more than 24 months, two (6.67%) admitted to being ill for 1–6 months, and another two (6.67%) admitted to being ill for 7-12 months. Sixteen (53.3%) subjects were considered within the normal weight range (18.5–24.9 kg/m^2), and only three of the subjects were obese (30.0–34.9 kg/m^2).

TABLE 1
Distribution of study sample based on gender, age, length of illness, BMI, liver stiffness, portal vein diameter and mean portal vein velocity

Variabel	Klasifikasi	N	%
Gender	Male	17	56.67
	Female	13	43.33
Age (years)	≤30	3	10
	31–50	8	26.7
	>50	19	63.3
Duration of illness (month)	1–6	2	6.67
	7–12	2	6.67
	13–18	–	–
	19–24	–	–
	>24	26	86.67
BMI (kg/m^2)	<18.5	5	16.67
	18.5–24.9	16	53.30
	25.0–29.9	6	20.00
	30.0–34.9	3	10.00
Liver stiffness (kPa)	10–15	10	33.3
	15–20	8	26.7
	20–25	3	10.0
	25–30	5	16.7
	>30	4	13.3
Portal vein diameter (mm)	<8	3	10.0
	8–10	6	20.0
	10–12	3	10.0
	12–14	14	46.7
	>14	4	13.3
Mean portal vein velocity (cm/s)	<15	4	13.33
	15–30	18	60.00
	30–45	5	16.67
	>45	3	10

Ten subjects (33.3%) had the result between 10–15 kPa when examined for liver stiffness, while 5 (16.67%) of them had the result of >30 kPa. Fourteen subjects' portal vein diameters were between 12–14 mm, while 3 subjects (10%) were <8 mm and another 3 were 10–12mm. Eighteen (60%) subjects were found with mean portal vein velocity between 15–30 cm/s, and only three (1-%) were found with >45 cm/s.

The results of the data normality test using the Shapiro-Wilk test showed that the liver stiffness variable, portal vein diameter, and mean portal vein velocity were not normally distributed (sig. > 0.05), leading Spearman to be used to analyze the correlation between the two variables.

The results of the Spearman test prove that there is no correlation between liver stiffness and portal vein diameter ($p = 0.250$, $r = -0.217$) and the mean portal vein velocity ($p = 0.883$, $r = -0.028$). There is no correlation between portal vein diameter and mean portal vein velocity with $p = 0.979$ and $r = -0.005$.

DISCUSSION

All chronic liver diseases, whether toxic, hereditary, autoimmune, or infectious, undergo typical histologic changes, ultimately leading to fibrosis/cirrhosis and excessive matrix deposition. Cirrhosis rapidly decompensates and has a high mortality rate. Patients with cirrhosis have reduced liver capacity to metabolize and synthesize proteins, peptides, and hormones. In addition, fibrosis progression and nodal regeneration cause an increase in portal vascular resistance with portal hypertension and an increase in the hepatic venous pressure gradient (HVPG) of 0.10 mmHg. Portal hypertension eventually leads to ascites and the development of vascular collaterals such as esophageal varices. Portal hypertension finally leads to ascites, and vascular collaterals will develop such as esophageal varices. Signs of these clinical features are what we look for when classifying liver disease patients with Child-Pugh classification. Even so, the patients in our study were of Child-Pugh A, whose liver dysfunction is still compensated. This may be why none of our results shows a correlation with one another.[14]

Liver stiffness can be affected by confounding factors such as hepatitis, mechanic cholestasis, liver congestion, cellular infiltrations, and deposition of amyloid irrespective of fibrosis stage. Patients with cholestatic liver diseases, such as primary biliary cirrhosis and primary sclerosing cholangitis, seem to have higher stiffness than those with viral hepatitis. Therefore, for each stage of fibrosis, cutoffs are higher than in chronic

TABLE 2
Spearmans test of liver stiffness, portal vein diameter, mean portal vein velocity

Spearman's rho		Liver stiffness	Portal vein diameter	Portal vein velocity
Liver stiffness	Correlation Coefficient	1.000	-.217	-.028
	Sig. (2-tailed)	.	.250	.883
	N	30	30	30
Portal vein diameter	Correlation Coefficient	-.217	1.000	.005
	Sig. (2-tailed)	.250	.	.979
	N	30	30	30
Portal vein velocity	Correlation Coefficient	-.028	.005	1.000
	Sig. (2-tailed)	.883	.979	.
	N	30	30	30

viral hepatitis either because of the nature of the liver disease or because of cholestasis. Similar higher cutoffs for each fibrosis stage were described in alcoholic liver disease. It should be mentioned that steatosis does not increase liver stiffness although it is often regarded as an essential initial state in chronic liver disease. Rather, steatosis may slightly decrease liver stiffness. As seen from our measurement data, our patients have varied levels of liver stiffness. This variety might affect the result of this research.[14,20]

Correlation between liver stiffness and the mean portal vein velocity

According to the Spearman test results, which were p=0.883 (p >0.05) and r = -0.028, there is no link between liver stiffness and the mean portal vein velocity. This is consistent with earlier research that linked liver stiffness to mean portal vein velocity such as Gunawan Y *et al.* (2022) which found no connection between liver stiffness and mean portal vein velocity and SWE. However, it disagreed with Sudirman I (2018), who demonstrated a weak correlation (r=0.271) between mean portal vein velocity as determined by ultrasonography and the degree of liver stiffness. Meanwhile, there is a significant correlation between the degree of fibrosis and the severity of fibrosis detected with SWE (p=0.001, r=0.672).[6,7]

Taking anti-hypertension medication may play a role. In this study, 4 of the subjects (10%) had been using propranolol for more than 3 months, and 15 (37.5%) had been using propranolol plus spironolactone. According to Amin *et al.* (2018), this can affect portal velocity in subjects because propranolol can lower portal pressure by reducing portal vein blood flow. This is associated with reduced cardiac output caused by the blockade of B1 adrenergic receptors.[8,9]

Correlation between liver stiffness and portal vein diameter

The results of this study showed no correlation between liver stiffness and portal vein diameter, measured at values of p=0.250 (p >0.05) and r = -0.217. This is consistent with previous studies that correlated the degree of hepatic stiffness with portal vein diameter, including Sudirman I (2018), which showed no significant relationship between portal vein di ameter and degree of hepatic stiffness (r = 0.166), but in contrast to Zaghloul S.G. (2019) who showed that changes in portal vein diameter are significantly correlated with liver stiffness.[6,10]

This may be due to several confounding factors beyond the investigator's control, such as the subjects' age and body weight. Ahmed M (2019) showed a significant correlation (r = 0.234; P=0.019 and r = 0.22; P=0.028) between portal vein diameter, age, and body weight, and Leao *et al.* (2012) showed that portal vein diameters were correlated significantly with age and BMI (p=0.02 and 0.001). Since the portal vein diameter rises with age with age and liver

Other variables that might affect the result are the level of subjects' ALT and the duration of their illness. An increase in portal vein diameter showed a statistically significant association with the duration of illness of more than six months (P <0.02) and increased serum alanine aminotransferase/ALT levels (P <0.03). Several studies have shown that increased aminotransferase levels are associated with higher shear wave velocity by virtual touch tissue quantification (VTQ) compared to that observed in patients with slightly elevated aminotransferases, which means that ALT serum level can also affect liver stiffness. The medication also played a part, as the mean portal vein diameter decreased significantly after 3 months of therapy with propranolol.

Propranolol is the most widely used non-selective beta blocker (NSBB) that causes a decrease in portal pressure due to reduced heart rate.[8,10,11]

Correlation between portal vein diameter and portal vein velocity

The results of this study showed that there is no correlation between portal vein diameter and mean portal vein velocity (p=0.979 (p >0.05) and r = 0.005). This is contrasting previous studies that show a correlation between portal vein diameter and the mean portal vein velocity, including Ahmed M (2019) (r=-0.628; P=0.0).[11]

Blood flow should be easier when there is no resistance, and velocity should be higher when the vein diameter is wider. This result might be influenced by previously mentioned factors that affect the portal vein. Further study might be necessary to confirm the hypothesis.

Limitations of the study

There were uncontrolled confounding factors in this study, including subjects' antihypertensive drug use (propranolol, bisoprolol, and spironolactone) over 3 months, age, BMI, disease duration, and serum ALT.

There are no cutoffs for liver stiffness grade, mean portal velocity, and portal diameter in this study because point SWE and ultrasonography are not the gold standards for diagnosis. Liver biopsy is the gold standard for assessing liver stiffness, but MR elastography is the best non-invasive method to assess liver stiffness. The gold standard test for portal hypertension is currently the HVPG.

CONCLUSION

This study proves that there is no correlation between portal vein dimensions and liver stiffness in patients with Child-Pugh A liver cirrhosis. Further research may be necessary with more controlled variables to confirm the hypothesis.

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