Original Article

Relationship between Hepatic Steatosis and Outcome of Viral Hepatitis C Treatment

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Background: Hepatitis C virus (HCV) infection is an important cause of liver disease. The correlation between hepatic steatosis and HCV treatment results is unclear. Majority of studies showed that hepatic steatosis decreases efficacy of treatment while some showed no correlation. Noninvasive modalities (transient elastrography; TE) have recently largely supplanted liver biopsy, which may limit recognition of steatosis. The controlled attenuation parameter (CAP) from TE is a parameter to identify hepatic steatosis.

Objective: To determine the correlation between hepatic steatosis and sustained virological response (SVR).

Materials and Methods: The retrospective study analyzed data from HCV infected patients in the hepatitis clinic of Hatyai Hospital between 2014 and 2017. All patients were measured for CAP before treatment. The correlation between hepatic steatosis and SVR was analyzed.

Results: Seventy four HCV infected patients participated in the present study. Twenty five percent of participants were hepatic steatosis (n = 15). SVR was 80% in hepatic steatosis group and 71.2% in group without hepatic steatosis (p = 0.50). Other factors showed no significant except significant fibrosis.

Conclusion: There was no relationship between hepatic steatosis and HCV treatment outcome.

Keywords: Controlled attenuation parameter, CAP, Hepatic steatosis, Outcome, Viral hepatitis C, Treatment

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Hepatitis C virus (HCV) infection is an important cause of liver disease affecting approximately 185 million patients worldwide[1]. HCV infection has been proven as the major cause of cirrhosis and hepatocellular carcinoma (HCC)[2]. Previous study revealed the positive association between hepatic steatosis and HCV infection in particular genotype 3[3], which is the most common genotype of HCV in Thailand[4].

The effect of steatosis on HCV treatment remained unclear. Many studies showed that histologic features of hepatic steatosis was associated with lower sustained virological response (SVR) rate[5,6]. However, some studies contradict showed that hepatic steatosis did not influence the efficacy of treatment[7].

Previously, most studies evaluated hepatic steatosis by liver biopsy, which is an invasive and potentially harmful procedure. Recently, noninvasive modality such as transient elastrography (TE) has supplanted liver biopsy. The controlled attenuation parameter (CAP) from TE has become a parameter to identify hepatic steatosis[8], though some investigators revealed the steatosis might be identified more often by CAP than by liver biopsy in HCV infected patients[9].

This research aimed to identify the relationship between hepatic steatosis diagnosed using CAP and HCV treatment results.

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Materials and Methods

Study population

This was a retrospective observational study of data gathered from the hepatitis clinic in Hatyai Hospital, a regional tertiary care hospital in south of Thailand, between January 2014 and December 2017. Inclusion criteria are detectable viral load HCV patients who measured pre-treatment CAP and receipt of complete treatment with interferon base regimen. Exclusion criterion is incomplete data of pre- and post-treatment data of HCV RNA viral load. The definition of hepatic steatosis is CAP ≥248 dB/m[8]. The significant fibrosis is fibrosis score ≥10 kPa[10] and the definition of cirrhosis is fibrosis ≥14 kPa[10]. All values were measured by a certified technician. Sustained virologic response (SVR) refers to undetectable HCV RNA VL at 24 weeks[10]. The duration of complete treatment with pegylated interferon plus ribavirin is 24 weeks for genotype 2,3 and 48 weeks for others.

The study was approved by the Institutional Review Board of Hatyai Hospital (Protocol number 115/2561).

Statistical analysis

Continuous data was presented as mean with standard deviation (SD) and significant differences between the two groups were assessed using Student's t-test. Categorical data was presented as number and percentage, and differences in data was analyzed using the Pearson Chi-square test or Fisher's exact test. The relationship between risk factors and outcome using Logistic regression. Statistical significance was taken as a *p*-value of less than 0.05. Statistical analyses were performed with STATA (version 15.1, College Station, TX: StataCrop LLC).

Results

A total of 74 patients were included in this study. There were 20 patients (27%), 46 patients (62.8%) and 8 patients (10.2%) of genotype 1, 3 and 6 respectively.

According to CAP, hepatic steatosis and non-hepatic steatosis group contained 15 (20.2%) and 59 (79.8%) participants, respectively. Demographic data were summarized in Table 1. There was no significant difference between the two groups except for underlying disease diabetes mellitus.

The authors analyzed the correlation between hepatic steatosis and SVR. Hepatic steatosis group had 12 patients who had SVR (80%). The non-hepatic steatosis group had 42 patients who had SVR (71.2%). This result showed no correlation between hepatic steatosis and SVR ($p = 0.50$) as shown in Figure 1.

Other factors have no correlation with SVR except significant fibrosis as shown in Table 2.

Discussion

Hepatic steatosis has been shown to relate with HCV infection, particularly genotype 3[3], which is the most common HCV genotype in Thailand[4]. Hepatic steatosis increases fibrosis in HCV infection by changing immune cells[11]. Therefore, HCV patients who have hepatic steatosis could have less satisfactory treatment results than those who do not[5,6,12]. However, our study did not support this hypothesis. Nevertheless, there were some previous studies that support our study result. For example, Rodriguez-Torres et al[7] showed hepatic steatosis did not influence the efficacy of HCV treatment. Their multivariate analysis revealed a confounding factor which is the baseline viral load.

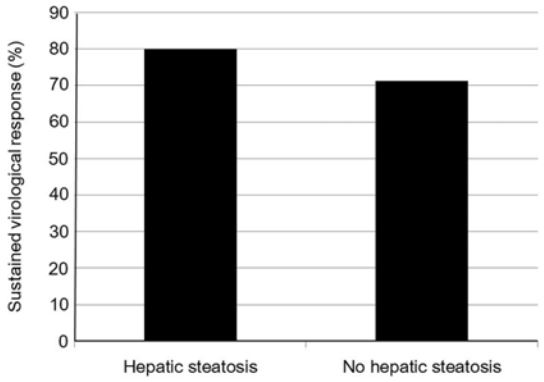

Figure 1. Sustained virological response rates between patients with and without hepatic steatosis.

Table 1. Baseline characteristics

Baseline characteristic	Hepatic steatosis (n = 15)	No hepatic steatosis (n = 59)	*p*-value
Male	11 (73.3)	46 (78.0)	0.74
Age (years), mean (SD)	47.9 (9.3)	46.5 (9.5)	0.61
Genotype 3	9 (60)	37 (62.7)	0.85
HCV viral load (x10^6 IU/mL), mean (SD)	5.1 (6)	2.8 (4.2)	0.19
BMI (kg/m^2), mean (SD)	24.3 (3.8)	22.5 (3.2)	0.06
History of intravenous drug use	5 (33.3)	18 (30.5)	1.00
HIV co-infection	3 (20)	23 (39)	0.17
Hepatitis B co-infection	1 (6.7)	0	0.20
Dyslipidemia	0	2 (3.4)	1.00
Diabetes mellitus	4 (26.7)	3 (5.1)	0.03
Significant fibrosis	12 (80)	37 (62.7)	0.21
Cirrhosis	7 (46.7)	27 (45.8)	0.95

Data are expressed as number (%), unless specified.
BMI = body mass index; HCV = hepatitis C virus; HIV = human immunodeficiency virus; SD = standard deviation

Table 2. Relationship between risk factors and outcome of treatment

Baseline characteristics	Univariate analysis			Multivariate analysis		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Steatosis	1.62	0.41 to 6.47	0.50	2.86	0.59 to 13.96	0.19
Male gender	0.50	0.13 to 1.99	0.33			
Genotype 3	2.00	0.71 to 5.68	0.19	2.65	0.85 to 8.27	0.09
History of IVDU	0.78	0.26 to 2.32	0.66			
Co-HIV infection	1.01	0.34 to 2.96	0.99			
Diabetes mellitus	0.45	0.09 to 2.23	0.33	0.41	0.60 to 2.56	0.34
Cirrhosis	1.20	0.42 to 3.41	0.73			
Significant fibrosis	0.26	0.07 to 0.98	0.05	0.22	0.06 to 0.90	0.04
Thrombocytopenia	1.14	0.32 to 4.07	0.84			
Transaminitis	1.05	0.32 to 3.45	0.93			

CI = confidence interval; HIV = human immunodeficiency virus; IVDU = intravenous drug user; OR = odds ratio

Of note, patients in hepatic steatosis group in this study comprised only 20% of the total number of patents studied, which was of lower proportion when compared to those of previous studies (40 to 85%)[13]. Hepatic steatosis could be affected by differences in the present study population, ethnicity and geographical area medical resources. Furthermore, there might be some biases in the patient selection for treatment. In Thailand, HCV infected patients must well controlled underlying disease e.g. dyslipidemia, diabetes mellitus, quit alcohol consumption before starting treatment.

In the present study, the authors found only one significant factor, significant fibrosis that correlated with treatment outcome. The presence of advanced liver fibrosis and cirrhosis has long been recognized to be associated with lower response rates to IFN-based treatment[14].

The advantage of our study was the use of less invasive technique, CAP, to diagnose hepatic steatosis as compared to previous approach using liver biopsy. However, there were some limitations of our study. First, the retrospective nature might cause selection bias and errors from data collection. Second, this study was conducted in a single regional tertiary center in southern part of Thailand, which may make it difficult to generalize this results nationwide.

Conclusion

Using CAP to evaluate hepatic steatosis, the present study showed no relationship between hepatic steatosis and outcome of HCV treatment.

What is already known in this topic?

HCV genotype 3 is the most common genotype in Thailand and percentage of hepatic steatosis in this genotype is more than other genotypes.

What this study adds?

This is the first study in Thailand that evaluates correlation between hepatic steatosis using CAP and HCV treatment results. The study shows no correlation between hepatic steatosis and result of HCV treatment.

Conflicts of interest

The authors declare no conflict of interest

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ความสัมพันธ์ระหว่างภาวะไขมันพอกตับกับผลการรักษาไวรัสตับอักเสบซี

กีรติ อัครปฏิมา, ทัศไนย สัตยรักษา, อรุณชัย แซ่ฉั่ง, อรรถพล รัตนสุภา

ภูมิหลัง: ไวรัสตับอักเสบ ซี เป็นโรคไวรัสตับที่มีความสำคัญ ความสัมพันธ์ระหว่างการมีไขมันพอกตับกับผลการรักษาของไวรัสตับอักเสบซี ข้อมูลยังไม่ได้ข้อสรุป ส่วนใหญ่มักเป็นไปในแง่การมีไขมันพอกตับทำให้การรักษาหายลดน้อยลงแต่มีบางงานวิจัยผลตรงกันข้าม มีข้อมูลว่าการเจาะตับมีข้อจำกัดในการประเมินภาวะนี้ ปัจจุบันจึงมีการใช้เครื่องมือ transient elastrography เข้ามาแทนที่เพื่อประเมินภาวะไขมันพอกตับโดยวัดค่า controlled attenuation parameter (CAP) ซึ่งบ่งบอกถึงภาวะไขมันพอกตับ

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างไขมันพอกตับกับผลการรักษาไวรัสตับอักเสบซี (sustained virologic response: SVR)

วัสดุและวิธีการ: ศึกษาข้อมูลย้อนหลังของผู้ป่วยไวรัสตับอักเสบซี จากเวชระเบียนผู้ป่วยนอกในคลินิกโรคตับ โรงพยาบาลศูนย์หาดใหญ่ ตั้งแต่ปี พ.ศ. 2557 ถึง พ.ศ. 2560 ผู้ป่วยทุกรายเข้ารับการวัดค่า CAP ก่อนเริ่มการรักษาวิเคราะห์ข้อมูลเปรียบเทียบความสัมพันธ์ระหว่างการมีไขมันพอกตับกับผลการรักษา

ผลการศึกษา: มีผู้ป่วยไวรัสตับอักเสบซี เข้าร่วมวิจัย 74 คน พบไขมันพอกตับ 15 คน คิดเป็นร้อยละ 25.4 โดยผู้ป่วยในกลุ่มที่มีไขมันพอกตับรักษาหายจากไวรัสตับอักเสบซี ร้อยละ 80 ส่วนกลุ่มที่ไม่มีไขมันพอกตับรักษาหายร้อยละ 71.2 ไม่ต่างกันอย่างมีนัยสำคัญทางสถิติ (ค่าพีเท่ากับ 0.50) ส่วนปัจจัยเสี่ยงอื่นๆ ไม่พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติยกเว้นการมีพังผืดตับที่มีนัยสำคัญ (significant fibrosis)

สรุป: ไม่พบความสัมพันธ์ระหว่างไขมันพอกตับกับผลการรักษาของไวรัสตับอักเสบซี