การลดลงของพังผืดในตับและภาวะแทรกซ้อนจากโรคตับในผู้ป่วยติดเชื้อไวรัสตับอักเสบซีที่ได้รับการรักษาจนหายขาด

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Abstract: Regression of Fibrosis and Liver Related Complications in Patients with Hepatitis C Who Achieved Sustained Virological Response

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(Received: 11 January, 2023; Revised: 21 March, 2023; Accepted: 28 July, 2023)

Background: Treatment with direct-acting antivirals (DAAs) eradicates hepatitis C virus from most patients. Information on regression of liver fibrosis and adverse outcomes is limited. **Objective:** The primary objective was to evaluate fibrosis changes in chronic hepatitis C (CHC) patients who achieved sustained virological response (SVR) with DAA-based therapy using transient elastography (TE). Secondary objectives were changes in non-invasive fibrosis scores; APRI and FIB-4, and liver and non-liver-related complications following SVR. **Methods:** This retro-prospective study was conducted at Rajavithi Hospital between June 2018 and June 2020. Consecutive CHC patients who achieved SVR with DAA were evaluated for TE, APRI, and FIB-4 under a standardized protocol at pre-treatment and follow-up periods of at least 12 months post-SVR. Fibrosis stages were categorized into F0/F1/F2/F3/F4. Fibrosis regression was defined as a reduction of the fibrosis stage after SVR. **Results:** Total of 104 patients were included with a mean follow-up of 20.5 (12-37) months. At pre-treatment, 74% had advanced fibrosis (F3-F4) with mean TE 18.8 kPa, FIB-4 3.4, and APRI 1.35. Following SVR, 61.5% had fibrosis regression, 35.6% had stationary fibrosis and 1.9% had fibrosis progression. Pre-treatment BMI≥25kg/m2 was significantly associated with less chance for fibrosis regression with an odd ratio of 2.34 (95%CI: 1.04, 5.25; p = .04), whereas HIV coinfection was significantly associated with a higher chance for fibrosis regression (p = .001). Two patients with de novo hepatocellular carcinoma were diagnosed at 14 and 39 months post-SVR (both had HCV genotype 3, obesity, and features of metabolic syndrome). There was no report of de novo hepatic decompensation and other significant liver and non-liver-related adverse events. **Conclusion:** Fibrosis regression was observed in most CHC patients after SVR and obesity was significantly associated with less chance to achieve fibrosis regression. Rare instances of de novo HCC were observed regardless of fibrosis status in which continuing surveillance should be recommended.

Keywords: HCV, SVR, Liver fibrosis

บทคัดย่อ

ภูมิหลัง: การรักษาไวรัสตับอักเสบซีด้วยยากลุ่ม direct acting antivirals (DAAs) ทำให้ผู้ป่วยหายขาดจากไวรัสตับอักเสบซีได้มาก ข้อมูลการลดลงของพังผืดในตับและผลการรักษาในระยะยาวยังคงมีจำกัด **วัตถุประสงค์:** วัตถุประสงค์หลักเพื่อประเมินการเปลี่ยนแปลงของพังผืดตับในผู้ป่วยไวรัสตับอักเสบซีที่ได้รับการรักษาจนหายขาดด้วยยา DAAs โดยการวัดค่าความยืดหยุ่นของเนื้อตับ วัตถุประสงค์รองเพื่อประเมินการเปลี่ยนแปลงของพังผืดตับด้วย APRI, FIB-4 รวมถึงศึกษาผลการรักษาในระยะยาว **วิธีการ:** การศึกษานี้เป็นการศึกษาแบบย้อนหลังที่รพ.ราชวิถี ผู้ป่วยไวรัสตับอักเสบซีที่ได้รับการรักษา จนหายขาดทุกรายจะได้รับการตรวจวัดค่าความยืดหยุ่นของเนื้อตับ, APRI และ FIB-4 ทั้งก่อนและหลังรักษา **ผล:** การศึกษานี้รวบรวมผู้ป่วย 104 ราย ระยะเวลาติดตามเฉลี่ย 20.5 เดือน ก่อนการรักษาพบร้อยละ 74 ของผู้ป่วยมีพังผืดตับ

ระยะที่ 3-4 มีค่าเฉลี่ยความยืดหยุ่นของตับ 18.8 kPa, FIB-4 3.4 และ APRI 1.35 หลังรักษาจนหายขาดพบว่าผู้ป่วยร้อยละ 61.5 มีพังผืดตับน้อยลง ร้อยละ 35.6 มีพังผืดตับคงที่ และร้อยละ 1.9 มีพังผืดตับมากขึ้น ดัชนีมวลกายที่มากกว่า 25 กก/ม.^{2} มีโอกาสพบการลดลงของพังผืดตับหลังการรักษาน้อยลง 2.34 เท่า (95%CI: 1.04, 5.25; p = .04) ผู้ป่วยสองรายพบมะเร็งตับหลังรักษา ทั้งสองรายติดเชื้อไวรัสตับอักเสบซีสายพันธุ์ที่ 3 และมีกลุ่มอาการอ้วนลงพุงก่อนการรักษา ไม่พบภาวะแทรกซ้อนอื่น ๆ ในงานวิจัยนี้ **สรุป:** ผู้ป่วยไวรัสตับอักเสบซีที่ได้รับการรักษาด้วยยากลุ่ม DAAs จนหายขาด ส่วนมากพบพังผืดในตับลดลงหลังการรักษา

คำสำคัญ: ไวรัสตับอักเสบซี, การรักษาจนหายขาด, พังผืดตับ

Introduction

Chronic hepatitis C virus (CHC) infection represents a major health problem globally with prevalence of 4-9% in Southeast Asia[1] and 2-4% in Thailand[2]. Since 2011, CHC infection is curable with direct acting antivirals (DAAs), so called sustained virological response (SVR) which means undetectable HCV-RNA after 12 weeks of treatment completion. In Thailand, DAAs has been approved in National list of Essential Drug in 2018, allowing more treatment access as well as higher SVR rates. By achieving this therapeutic milestone, risks of hepatic and extrahepatic complications from CHC infection, hepatic decompensation, liver-related mortality, as well as risk of hepatocellular carcinoma (HCC) are substantially reduced. Fibrosis stage has been known as the very important prognostic indicator of chronic liver disease including CHC. Liver biopsy has been used as the standard tool for assessing liver fibrosis, however, in the past decade, several non-invasive markers for liver fibrosis have been introduced and demonstrated a reasonable ability to identify the stage of liver fibrosis. Transient elastography (TE) is one of the most widely-validated tool to evaluate fibrosis status as well as in patients with chronic liver diseases including CHC[3-5]. Notably, serum non-invasive fibrosis markers and scores have also been studied to evaluate fibrosis status in CHC patients, for example, Fibrotest®, Forns index, APRI, FIB-4, etc[6-7]. Due to their non-invasive nature and availability, these tests are becoming favored means to assess fibrosis status used in treatment initiation as well as longitudinal follow-up in many centers. Previous studies have demonstrated that liver fibrosis can be regressed, or even reversed, after viral clearance with DAAs treatment. A meta-analysis of 24 studies in 2934 CHC patients (2214 patients achieved SVR) showed significant fibrosis regression in patients who achieved SVR with higher magnitude in studies with longer follow-up duration[8]. A recent prospective study in 2326 Egyptian patients showed more than half of patients with advanced fibrosis (F3-F4) achieved fibrosis regression at 2-year follow-up[9]. However, the risk of hepatic decompensation is not absolutely eliminated after cure of CHC, continuing surveillance for adverse events, especially the occurrence of HCC is still recommended. American Association for the Study of Liver Diseases (AASLD) and European Association for the Study of the Liver (EASL) recommend indefinite twice-yearly ultrasounds surveillance in patients with advanced fibrosis (F3 or F4 by METAVIR staging), even after SVR is achieved[10-11]. This lifelong approach not only causes burden to patients and physicians, but also to national health economics. Several recent studies have been conducted to explore potential associated factors of liver-related and non-liver-related events in CHC patients post-SVR, yet most studies were conducted in western populations while studies in Asian populations with different genotypic distribution as well as lifestyle, comorbidities, and other characteristics were still limited. This study aimed to study fibrosis regression as well as liver- and non-liver-related adverse outcomes in CHC patients post-SVR in Thailand.

Materials and Methods

This was a retro-prospective observational cohort study including 104 CHC patients receiving DAAs in the out-patient clinics at Rajavithi Hospital, Bangkok, Thailand from June 2018 to June 2020. Our inclusion criteria were CHC-infected patients, 18 to 70 year of age who received DAAs-based treatment and achieved SVR12. Patients with HCC were included only if no evidence of residual/ recurrent tumor documented within 6 months after SVR. Patients with other malignancies, renal impairment, uncontrolled medical illness, terminal illness, current alcohol drinking, uncontrolled depression, pregnancy, HBV coinfection, history of liver transplantation, and hepatic decompensation (Child Turcotte Pugh score more than 7) were excluded. All patients were evaluated for basic laboratory tests,

hepatitis C genotype, HCV-RNA (viral load), and TE prior to treatment. Ultrasonography and serum AFP were performed in all consecutive patients to confirm the absence of HCC and triphasic multidetector computed tomography (MDCT) was subsequently performed in every suspicious lesion. Patients were followed up every 4 weeks since treatment initiation till treatment completion and 12 weeks after treatment completion for confirmation of SVR. Those who achieved SVR for minimum 12 months were evaluated for fibrosis regression by TE, non-invasive fibrosis scores, liver-related and non-liver-related complications, as well as other serum markers. TE and controlled attenuation parameter (CAP) were done using Fibroscan® (Echosen, Paris) under a standardized protocol by an experienced (>150 cases per year) and certified operator both before treatment initiation and during follow-up period. Liver-related complications were defined as any decompensated events, liver failure, and occurrence of HCC post-SVR. Non-liver related complications referred to any complications not related to chronic liver disease for example, other malignancy, cardiovascular events, etc. We defined fibrosis regression as any reduction of liver fibrosis stages post treatment. Patients who failed to achieve fibrosis regression were those who stay at the same fibrosis stage and those with fibrosis progression. We used changes in fibrosis stages rather than absolute change in TE to better understand the magnitude of fibrotic change; F1 ≤ 7 kPa, F2 ≤ 9.4 kPa, F3 ≤ 12.4 kPa, F4 > 12.4 kPa[12]. We further classified our patients according to the degree of fibrosis regression as followed: cirrhosis reversal, defined by a decrease of fibrosis by two or more stages; fibrosis regression, defined as a decrease of fibrosis by only one stage; stationary fibrosis, defined as no change of fibrosis stage; and fibrosis progression, defined as an increase of any fibrosis stage. Non-invasive liver fibrosis scores used in this study were Fibrosis-4 (FIB-4) score[13] and APRI (aspartate aminotransferase-to-platelet ratio)[14]. DAAs regimens were individually selected for each patient according to hepatitis C genotype and pre-treatment fibrosis status in accordance with Thailand National treatment guideline during the treatment period. Ribavirin was added in every patient with TE more than 12 kPa. The primary endpoint analyzed was the changes in hepatic fibrosis stages after achieving SVR with DAAs-based therapy in HCV patients using transient elastography (TE). Secondary outcomes were changes of non-invasive fibrosis scores; APRI and FIB-4, liver and non-liver-related complications, and factors associated with fibrosis regression and complications.

The sample size was calculated based on incidence of fibrosis regression of 0.51 as previously reported in Shiha G, et al[9]. Assuming a type I error of 5% ($p < .05$) and a type II error of .20 (80% power), a total sample size of at least 97 patients needed to be enrolled in the study. Statistical analyses were performed using version 22, SPSS (Statistical Package for Social Sciences) (IBM Corp., USA). Continuous variables were reported as mean (SD). Categorical variables were reported as frequency (%). Paired analysis was done by paired *t* test. For comparisons, the chi-square test was used for categorical variables and ANOVA test and independent *t* test were used for continuous variables, as appropriate. Variables with nonnormal distribution are expressed as median and interquartile range (IQR) and were compared using the Wilcoxon signed rank test. Statistical significance was defined as $p < .05$.

Results

One-hundred and four CHC infected patients who achieved SVR with DAAs -based therapy were included. Detailed patient characteristics, laboratory values, TE and non-invasive fibrosis scores were shown in Table 1. Among the included patients, 27 patients belonged to null-early fibrosis stages (F0-F2), while 77 patients belonged to advanced stages (F3-F4) classified according to baseline TE. The mean follow-up period since SVR achievement was 20.67 (5.78) months (minimum and maximum of 12 and 37 months, respectively) and 51.9% of included patients had long follow-up period of more than 24 months post-SVR.

Table 1 Baseline Characteristics (n = 104)

Factors	Total (n = 104)	F0-2 (n = 27)	F3 (n = 17)	F4 (n = 60)	p-value
Age	53.63 ± 8.91	49.89 ± 9.88	52.29 ± 11.04	55.7 ± 7.16	.014*
Male	79 (76.0)	21 (77.8)	14 (82.4)	44 (73.3)	.720
BMI pretreatment	25.14 ± 4.34	24.13 ± 2.83	24.53 ± 4.62	25.76 ± 4.76	.222
Metabolic syndrome	49 (47.1)	10 (37)	8 (47.1)	31 (51.7)	.449
Fatty liver	18 (17.3)	6 (22.2)	3 (17.6)	9 (15.0)	.712
HIV coinfection	16 (15.4)	7 (25.9)	4 (23.5)	5 (8.3)	.065
Alcohol consumption					.470
Never	64 (61.5)	20 (74.1)	10 (58.8)	34 (56.7)	
<50 gm/week	14 (13.5)	4 (14.8)	3 (17.6)	7 (11.7)	
≥ 50 gm/day	3 (2.9)	0 (0.0)	0 (0.0)	3 (5.0)	
History of ≥ 50 gm/day	23 (22.1)	3 (11.1)	4 (23.5)	16 (26.7)	
coffee consumption	14 (13.5)	4 (14.8)	2 (11.8)	8 (13.3)	.958
TE	18.79 ± 13.22	7.8 ± 1.33	11.04 ± 0.81	25.94 ± 13.41	<.001*
CAP (dB/m)	226.78 ± 48.75	221.26 ± 39.32	222 ± 50.28	230.62 ± 52.40	.648
AST	82.14 ± 53.15	79.3 ± 45.81	69 ± 35.20	87.15 ± 59.94	.443
ALT	83.86 ± 64.10	78.81 ± 43.32	60.94 ± 34.92	92.62 ± 76.00	.178
Albumin	4.28 ± 0.48	4.18 ± 0.57	4.31 ± 0.30	4.32 ± 0.47	.419
TB	0.83 ± 0.39	0.85 ± 0.41	0.72 ± 0.33	0.85 ± 0.40	.442
Platelet count ($x10^3$)	189.50 ± 69.24	177.41 ± 49.52	223.18 ± 88.61	185.40 ± 68.90	.079
INR	1.08 ± 0.09	1.08 ± 0.09	1.05 ± 0.09	1.08 ± 0.09	.512
FIB4	3.43 ± 3.88	1.64 ± 0.78	1.66 ± 0.80	4.74 ± 4.66	<.001*
APRI	1.35 ± 1.20	0.56 ± 0.34	0.61 ± 0.30	1.92 ± 1.30	<.001*

Value are represented as number(%), Mean±SD, *significance at p<.05

Of 104 patients included in our study, 64 patients (61.5%) showed fibrosis regression: 25 patients wit cirrhosis reversal and 39 patients with fibrosis regression. The remaining 37 patients (35.6%) were stationary compared with pretreatment fibrosis stage, and only 2 patients (1.9%) had fibrosis progression (Figure 1). In 60 cirrhotic patients (F4 before treatment), 16 patients (25.81%) showed reversal of hepatic fibrosis to F2 or less, 13 patients (20.96%) showed only one stage improvement to F3 (fibrosis regression) while 31 patients (50%) remained F4 with no change in fibrosis stage (stationary). Proportion of patients with advanced fibrosis significantly reduced following SVR; from 74% to 45.2%. Detailed changes in fibrosis stages post-SVR are shown in Figure 2. Non-invasive fibrosis scores: APRI and FIB-4, significantly reduced with median reduction of 0.6 (0.2-1.2) and 0.77 (0.2-2), respectively. Serum AST, ALT, and platelet count showed significant improvement post-SVR. There were 2 patients with new HCC and 1 patient with recurrent HCC during follow-up period while other liver-and non-

liver-related complications were not observed in this study. Pre-treatment BMI≥25kg/m2 was significantly associated with less chance for fibrosis regression post-SVR with odd ratio 2.34 (95%CI: 1.04, 5.25; p = .04), whereas HIV coinfection was significantly associated with higher chance for fibrosis regression (p = .001).

Table 2 Changes in BW, BMI, laboratory values, and non-invasive fibrosis scores of all patients between baseline and last available follow-up

Factors	Pre (n = 104)	Post (n = 104)	p-value
BMI (kg/m^2)	25.14 ± 4.34	25.16 ± 4.14	.913
Transient elastography	18.79 ± 13.22	11.91 ± 9.18	<.001*
CAP	226.78 ± 48.75	232 ± 42.89	.212
AST	82.14 ± 53.15	33.19 ± 15.43	<.001*
ALT	83.86 ± 64.10	28.66 ± 16.04	<.001*
Platelet count (x10^3)	189.50 ± 69.24	213.13 ± 79.12	<.001*
INR	1.08 ± 0.09	1.06 ± 0.08	.060
FIB-4	3.43 ± 3.88	2.1 ± 2.73	<.001*
APRI	1.35 ± 1.20	0.47 ± 0.33	<.001*

Value are represented as number(%), Mean±SD, * significance at p<.05

CAP = Community-acquired Pneumonia, AST = aspartate aminotransferase, ALT = Alanine transaminase, INR = International Normalized Ratio, FIB-4 = Fibrosis-4, APRI = AST to platelet ration index

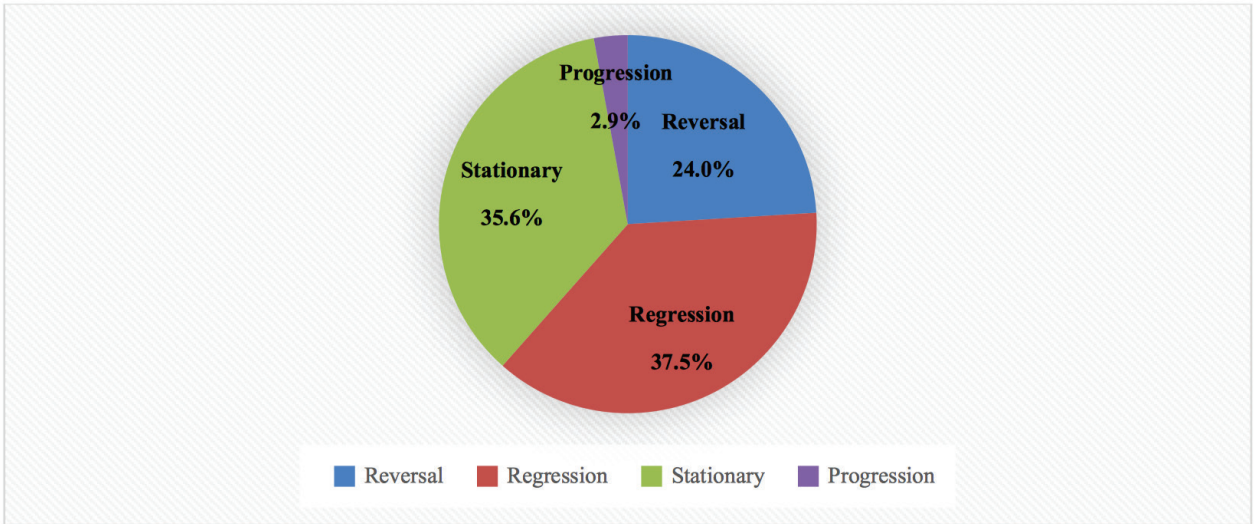

Figure 1 Percentages of posttreatment fibrosis changes in CHC-infected patients

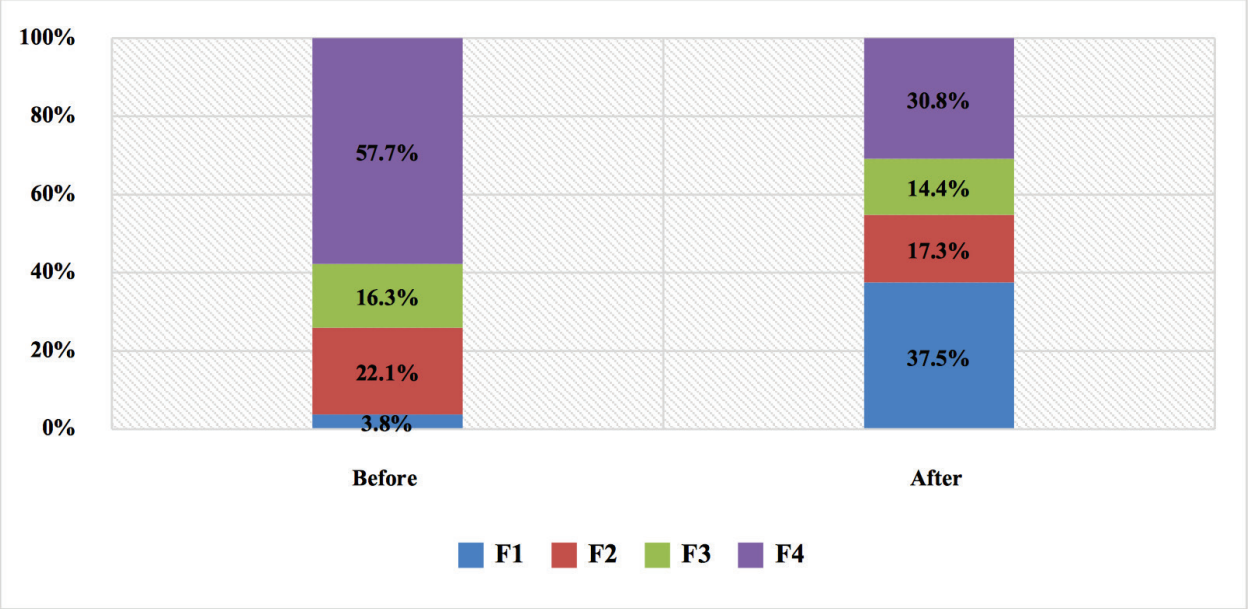

Figure 2 Changes in fibrotic stages in post-SVR CHC patient

Table 3 Pretreatment characteristics of patients classified in post-treatment changes in liver fibrosis

Factors	Total (n = 104)			F3-F4 (n = 77)		
	Fibrosis regression (n = 64)	No fibrosis regression (n = 40)	p-value	Fibrosis regression (n = 44)	No fibrosis regression (n = 33)	p-value
Age	52.56 ± 9.43	55.35 ± 7.83	.121	54.14 ± 9.08	56.03 ± 6.89	.320
Male	50 (78.1)	29 (72.5)	.514	35 (79.5)	23 (69.7)	.321
BMI pretreatment	24.77 ± 4.72	25.72 ± 3.64	.280	24.98 ± 5.44	26.17 ± 3.53	.251
BMI ≥ 25 kg/m^2	25 (39.1)	24 (60.0)	.037*	17 (38.6)	22 (66.7)	.015*
Metabolic syndrome	30 (46.9)	19 (47.5)	.950	23 (52.3)	16 (48.5)	.742
Fatty liver	14 (21.9)	4 (10.0)	.119	9 (20.5)	3 (9.1)	.174
HIV coinfection	16 (25.0)	0 (0.0)	.001*	9 (20.5)	0 (0.0)	.006*
Black coffee consumption (cups)	8 (12.5)	6 (15.0)	.716	5 (11.4)	5 (15.2)	.625
Transient elastography	14.71 ± 9.88	25.33 ± 15.27	<.001*	17.67 ± 10.69	29.29 ± 13.8	<.001*
Fibrosis stage			<.001*			.003*
1	0 (0.0)	4 (10.0)		0 (0.0)	0 (0.0)	
2	20 (31.3)	3 (7.5)		0 (0.0)	0 (0.0)	
3	15 (23.4)	2 (5.0)		15 (34.1)	2 (6.1)	
4	29 (45.3)	31 (77.5)		29 (65.9)	31 (93.9)	
CAP pretreatment	230.28 ± 49.56	221.18 ± 47.5	.357	235.16 ± 52.09	220.12 ± 50.77	.209
Albumin	4.25 ± 0.48	4.34 ± 0.47	.348	4.3 ± 0.39	4.35 ± 0.49	.639
TB	0.8 ± 0.34	0.88 ± 0.46	.306	0.8 ± 0.33	0.85 ± 0.46	.572

Table 3 Pretreatment characteristics of patients classified in post-treatment changes in liver fibrosis (continue)

Factors	Total (n = 104)			F3-F4 (n = 77)		
	Fibrosis regression (n = 64)	No fibrosis regression (n = 40)	p-value	Fibrosis regression (n = 44)	No fibrosis regression (n = 33)	p-value
Platelet count ($x10^3$)	196.39 ± 70.414	178.48 ± 66.69	.201	201.70 ± 76.56	183.12 ± 72.04	.283
INR	1.07 ± 0.08	1.09 ± 0.10	.173	1.06 ± 0.07	1.09 ± 0.1	.092
FIB-4	2.06 ± 1.25	5.63 ± 5.41	<.001*	2.37 ± 1.35	6.32 ± 5.72	<.001*
APRI	0.83 ± 0.56	2.2 ± 1.46	<.001*	0.97 ± 0.59	2.51 ± 1.41	<.001*

Values are represented as number (%), Mean±SD, * significance at p<.05

CAP = Community-acquired Pneumonia, INR = International Normalized Ratio, FIB-4 = Fibrosis-4, APRI = AST to platelet ration index

Discussion

This study included 104 CHC patients who achieved SVR with DAAs-based therapy and followed for minimum of 1 year[3-5]. TE is a composite of tissue inflammation and fibrotic deposition, it may "overestimate" fibrosis reversal from inflammatory process in acute phase, making fibrosis status or fibrosis regression hardly reliable in early period post-SVR, we extended the first follow-up period to 12 months post-SVR, when inflammatory processes subsided. In concordance with previous studies, fibrosis regression, evaluated by TE, APRI, and FIB-4, was observed in most CHC patients following SVR[9]. Median of changes in TE and the proportion of patients with significant fibrosis regression were 2.5 kPa and 74% in patients with baseline null-early fibrosis, and 6.8 kPa and 57.1% in those with advanced fibrosis, respectively. Lledo GM, et al[15] studied 260 CHC patients treated with DAAs in Spain (57.2% with advanced fibrosis). A significant fibrosis regression at SVR12 was seen in 40%, being more frequent in patients with baseline advanced fibrosis than in those with early fibrosis (52.3 vs 22.5%; $p < .001$). In addition, Pietsch V, et al conducted a study in 143 German patients with a longer follow-up duration of 96 weeks, regression of liver fibrosis was also more prominent in patients with advanced fibrosis[16]. Our study, on the other hand, showed fibrosis improvement in 74.7% of patients with null-early fibrosis and 57.14% in patients with advanced fibrosis. This might be explained by different ethnic background, genotypic distribution, and duration of follow-up. Therefore, to better understand the degree of fibrosis regression in patients with early fibrosis, further studies are required. There was no report of de novo hepatic decompensation, liver-related mortality, and non-liver-related complications in our study, possibly due to our relatively small sample size, particularly for patients with advanced liver disease, and short follow-up period. Mendizabal M, et al. showed cumulative incidence of disease progression as defined by liver decompensation events, de novo HCC, need for liver transplantation, and death, was 3.6% (95% CI, 2.7%, 4.7%) in a study of 1366 post-SVR CHC patients with a median follow-up period of 26.2 months[17]. HCC is known to be the very important liver-related event in patients with CHC-related cirrhosis cured by DAAs[18]. A 6-year follow-up study including 25,424 CHC patients in the United States by Ioannou GN, et al previously showed HCC incidence post-SVR with DAAs-based therapy was 0.92 per 100 patient-years[19]. Another study in 1,270 cirrhotic French patients with mean follow-up duration of 3 years showed 5.9% incidence of HCC in SVR patients treated with DAAs[20]. De novo HCC was found in 2 patients in our study.

Advanced age and presence of comorbidities, such as metabolic syndrome, alcohol abuse, and HIV coinfection, have been shown to influence liver fibrosis progression[21]. We thus hypothesized these factors might have some effects toward fibrosis regression in post-SVR CHC patients. The presence of HIV infection and BMI≥25kg/m^2 showed significant effect toward fibrosis regression in our study; patients with BMI≥25kg/m^2 were associated with less fibrosis improvement while HIV-coinfection was associated with more fibrosis regression with all HIV-CHC co-infected patients achieved improvement

in fibrosis regardless of baseline liver fibrosis status. In concordance to previous studies, obesity, liver steatosis and metabolic syndrome had shown to enhance fibrosis progression in CHC patients[22]. However, it was surprising since HIV infection was also earlier known to accelerate the rate of fibrosis progression in CHC patients, especially in those with low CD4 count[23]. Notably, our study included only HIV-infected individuals who had been virally suppressed with high CD4 count; postulated that they had good compliance to medications as well as relatively good health concerns. This group of patients, as well, need frequent follow-up in infectious clinics; medical advice, laboratory check, and health awareness might be better provided. Further studies are required to clearly evaluate the potential influence of HIV infection to fibrosis progression post-SVR.

To our knowledge, we are the first study in Thailand evaluating CHC patients achieving SVRs with DAAs-based regimen. Data regarding fibrosis regression in CHC patients in Southeast Asia, with different ethnic background and genotypic distribution, was also limited. The strengths of our study were that only two experienced and certified operators under the single machine (Fibroscan®) and standard protocol were assigned to evaluate fibrosis status both pre- and post-treatment in our study population, lessening potential bias from this operator-dependent procedure. Our follow-up period was at least 12 months post-SVR, eliminating potential interference from reduction of inflammatory process in early period post-treatment.

Our study also has several limitations. Firstly, we have relatively small sample size. Our study is single-centered, validation of our findings might be needed in other patient populations. The mean follow-up period was 20.67 (5.78) months post-SVR, which might be insufficient to evaluate liver-related adverse events in non-advanced liver disease population as well as their potential predictors. Lastly, our study is partly retrospective, making uncontrolled bias unavoidable.

In conclusion, Fibrosis regression was observed in most CHC patients after SVR regardless of pre-treatment fibrosis status. Obesity was significantly associated with less chance to achieve fibrosis regression. Rare instances of de novo HCC were observed in which continuing surveillance following SVR may be required.

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