ORIGINAL ARTICLE

Virologic responses and tolerance of peginterferon alfa plus ribavirin treatment for patients with chronic hepatitis C virus infection in different age categories

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Abstract

Objective: This study aimed to evaluate the effect of age on the treatment comprising peginterferon plus ribavirin administered to patients with chronic hepatitis C (CHC).

Materials and Methods: A total of 314 patients with CHC treated with peginterferon plus ribavirin were classified into three categories according to age. The efficacy and safety outcomes were compared between groups.

Results: Elderly patients yielded significantly lower rapid virological response and sustained virological response (SVR) (31.3% and 35.4%, respectively, $P < 0.05$) rates than younger patients. The discontinuation rate of the patients aged ≥ 60 years were significantly higher (29.2%, $P = 0.004$) than that of the younger patients. The elderly patients suffered from adverse events, such as fatigue ($P = 0.005$), neutropenia ($P = 0.013$), jaundice ($P = 0.013$), hepatocellular carcinoma ($P = 0.013$), and gastric cancer ($P = 0.018$), more frequently than the younger patients. In multivariable analysis, age was a negative factor that affected the SVR of the patients with CHC (odds ratio [OR] =0.983, 95% confidence interval [95% CI] =0.967–1.0, $P = 0.05$). The SVR rate of the patients with hepatitis C virus (HCV) genotype non-1 was significantly higher than that of the patients with HCV-1 (OR = 0.559, 95% CI = 0.349–0.895, $P = 0.015$). An early virological response could be considered as a powerful positive predictor to obtain an SVR (OR = 2.353, 95% CI = 1.411–3.922, $P = 0.001$).

Conclusions: Increasing age negatively affected the efficacy of peginterferon and ribavirin therapy in the treatment of patients with CHC. Elderly patients experienced poorer treatment tolerance and adherence, and as a result, treatment efficacy is poor.

Key words: Aged, chronic, hepatitis C, peginterferon, ribavirin, sustained virological response

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Introduction

Chronic hepatitis C virus (HCV) infection has caused heavy social and economic burden worldwide over the past decades.[1-4] The prevalence of this infection increases with age, particularly in industrialized countries, such as Japan and Italy.[5,6] In Taiwan, the peak anti-HCV seroprevalence rate is observed among people aged between 60 and 80 years.[7] A survey in the United States has revealed an anti-HCV prevalence of 0.9% among persons aged 60 years and above.[8] The rate of cirrhosis development is higher in older patients with chronic hepatitis C (CHC) than in

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younger patients. The prevalence of cirrhosis also increases with age.[9,10]

Although triple therapy with either telaprevir or boceprevir is used as the standard care treatment for patients infected with HCV genotype 1 in some developed countries, peginterferon plus ribavirin therapy is considered as the first-line regimen to treat patients with CHC.[1-3] However, the administration of this therapy among elderly patients is limited because of the lack of data on its efficacy and tolerability. In a prospective cohort study of Tsui *et al*.,[11] 9% of 4025 patients screened throughout the United States are classified as elderly. Approximately 25% of these elderly patients are considered as treatment candidates by an evaluating clinician, but only 10% of these patients have received the treatment. After comorbidities are adjusted, old age remains associated with a lower likelihood of becoming a treatment candidate.[12] However, these patients usually require aggressive treatment because they are at a high risk of disease progression.[10,13,14]

This retrospective study was designed to evaluate the treatment response and safety profile of the peginterferon plus ribavirin treatment for elderly patients with CHC and to identify the potential factors associated with the sustained virological response (SVR) in this population.

Materials and Methods

Patients

This retrospective study was conducted by the Shanghai Public Health Clinical Center, Fudan University, Shanghai, China. A total of 314 naive patients with CHC were enrolled between September 2009 and September 2013. All patients were treated with peginterferon plus ribavirin. Patients were excluded if they decompensated cirrhosis or other forms of liver diseases, such as autoimmune hepatitis, coinfection with hepatitis B, or anti-human immunodeficiency virus. The study protocol and the informed consent forms were reviewed and approved by the Ethics Committee of the Shanghai Public Health Clinical Center, Fudan University, Shanghai, China. At the beginning of their hospitalization, all of the patients provided their written consent to allow their information to be stored in the hospital database and to be used for the research. Our experiments were conducted in China.

Treatment

All of the patients received weekly doses of 180 μg of peginterferon alfa-2a (Pegasys, Hoffmann-La Roche, Shanghai, China) or 1.5 μg/kg peginterferon alfa-2b (Peg-Intron, Schering Plough Corporation, Kenilworth, NJ, USA). Ribavirin was administered at daily doses of 600–1000 mg depending on the body weight of the patients (600 mg/day for patients weighing <60 kg, 800 mg/day for patients weighing 60–75 kg, and 1000 mg/day for patients weighing >75 kg). Treatment was administered to patients with HCV genotype 1 for 48 weeks and to those with genotype 2, 3, or 6 for 24 weeks. Treatment was discontinued when the hemoglobin (Hb) concentration of a patient declined below 85 g/L because of drug-induced anemia, when the neutrophil count declined below 500/mm^3, or when the platelet count declined below 25,000/mm^3. Some patients discontinued treatment because the virus could not be eradicated after 12 or 24 weeks, as determined by a physician. The dose of ribavirin was reduced to 600 mg/day when the Hb concentration of a patient declined below 100 g/L because of drug-induced anemia. All of the patients received 40 mg of leucogen tablets (Jiangsu Jibeier Pharmaceutical Corporation Limited, Jiangsu, China) three times a day after the combined therapy was administered to prevent drug-induced neutropenia, anemia, and/or thrombocytopenia.

Virological assessment and definition of virological response

The serum antibodies for HCV were detected by a third-generation HCV enzyme-linked immunosorbent assay (Axsym HCV, version 3.0, Abbott Laboratories, Abbott Park, IL, USA). The serum RNA level of HCV was measured through a quantitative real-time polymerase chain reaction assay (Applied Biosystems 7500 real-time PCR system; Applied Biosystems, Atlanta, USA). Rapid virological response (RVR) was defined as an undetectable serum HCV RNA at week 4, early virological response (EVR) was defined as ≥2 log reduction or complete absence of HCV RNA at week 12 compared with the baseline, end-to-treatment virological response (ETR) was defined as the undetectable virus at the end of either a 24- or 48-week therapy, and SVR was defined as undetectable serum HCV RNA 24 weeks after the treatment.

In accordance with the protocol, genotype 1 patients with less than a 2 log decrease in HCV RNA level at week 12 compared with the baseline or with detectable serum HCV RNA at week 24 stopped taking the treatment and were regarded as nonresponsive. Treatment discontinuance was evaluated except for those patients who discontinued the treatment in 24 weeks because of the absence of a response. Anti-viral efficacy was evaluated through intention-to-treat (ITT) analysis for all patients and through per protocol (PP) analysis for those patients conducted complete treatment duration.

Statistical analysis

Parametric data were expressed as mean ± standard deviation or median values. Kolmogorov–Smirnov test was conducted to evaluate normality; Student's *t*-test was performed to compare the means of normally distributed continuous data, Mann–Whitney U-test was employed to evaluate the nonnormally distributed continuous data, and Chi-squared test was used to analyze categorical variables. The factors that were associated with viral response were assessed via univariable and multivariable analyses through logistic regression analysis. Only those covariates that were significantly associated with SVR at univariable analysis (two-sided $P < 0.10$) were shown and included in the multivariate model. Data were reported as odds ratios (ORs) with 95% confidence intervals (95% CIs).

Statistical analyses were performed using PASW Statistics version 18.0 (SPSS Inc., Chicago, IL, USA). All *P* values were two-tailed, and differences with $P < 0.05$ were considered statistically significant.

Results

Patient characteristics

A total of 314 patients with chronic HCV infection who

Table 1: Baseline characteristics of patients

Characteristics	Total (*n*=314)	Age group (years)			*P*
		<40 (*n*=121)	40-59 (*n*=145)	≥60 (*n*=48)	
Gender, male (%)	204 (65.0)	91 (75.2)	85 (58.6)	28 (58.3)	0.011
Exposure category, *n* (%)					<0.001
Injection drug use	51 (16.2)	37 (30.6)	14 (9.7)	0 (0)	<0.001
Blood transfusion	140 (44.6)	26 (21.5)	84 (57.9)	30 (62.5)	<0.001
Other	123 (39.2)	58 (47.9)	47 (32.4)	18 (37.5)	0.035
Body weight, *n* (%)					
<60 kg	16 (5.1)	6 (5.0)	7 (4.8)	3 (6.3)	0.884
60-75 kg	180 (57.3)	70 (57.9)	77 (53.1)	33 (68.8)	0.158
≥75 kg	118 (37.6)	45 (37.2)	61 (42.1)	12 (25.0)	0.106
Diabetes, *n* (%)	36 (11.5)	2 (1.7)	18 (12.4)	16 (33.3)	<0.001
Hypertension, *n* (%)	24 (7.6)	1 (0.8)	10 (6.9)	13 (27.1)	<0.001
Alcohol consumption[#], *n* (%)	14 (4.6)	8 (7.2)	6 (4.1)	0 (0)	0.151
Genotype, *n*					
1	159 (50.6)	63 (52.1)	72 (49.7)	24 (50.0)	0.922
2/3/6	155 (49.4)	58 (47.9)	73 (50.3)	24 (50.0)	
HCV RNA (median, $\log_{10}$ IU/mL)	204 (65.0)	6.37 (3.03-7.69)	6.52 (3.01-7.84)	6.77 (3.68-7.55)	0.532
ALT (IU/L)	83 (14–1207)	104.5 (14-1207)	76 (18-689)	57 (18-431)	0.001
Aspartate aminotransferase (IU/L)	51 (16.2)	49 (12-423)	55 (16-227)	61 (19-241)	0.764
Neutrophil count (cells/mm^3)	140 (44.6)	2.78 (1.27-5.75)	2.45 (0.75-6.31)	2.31 (1.10-4.44)	0.001
Hemoglobin (g/L)	123 (39.2)	147.4 (87.0-170.2)	140.1 (77.0-172.0)	133.7 (104.8-152.7)	<0.001
Platelet count (cells/mm^3)	153.1±66.0	185.5 (61.0-475.0)	134.0 (29.0-284.0)	107.5 (52.0-396.0)	<0.001
Creatinine (μmol/L)	16 (5.1)	71.80±12.59	65.81±13.13	67.72±16.53	0.007
Total cholesterol (mmol/L)	180 (57.3)	3.75±0.86	3.92±0.83	3.89±0.90	0.328
Total glycerol (mmol/L)	118 (37.6)	1.01 (0.35-2.25)	1.11 (0.34-13.03)	0.94 (0.56-1.96)	0.124
High density lipoprotein (mmol/L)	36 (11.5)	1.24 (0.71-2.69)	1.20 (0.26-2.68)	1.20 (0.71-2.14)	0.929
Low density lipoprotein (mmol/L)	24 (7.6)	2.17±0.78	2.32±0.70	2.34±0.69	0.292
Liver histology (metavir score)[Δ], *n* (%) (F 3-4 and/or A 2-3)	14 (4.6)	2 (1.7)	16 (11.0)	9 (18.8)	<0.001

[#]Alcohol consumption>20 g/day during the past 6 months before treatment; [Δ]27 patients managed liver biopsy. F0-F4 (F0=No fibrosis; F1=Portal fibrosis without septa; F2=Few septa; F3=Numerous septa without cirrhosis; F4=Cirrhosis); A0-A3 (A0=No histological activity; A1=Mild activity; A2=Moderate activity; A3=Severe activity). HCV=Hepatitis C virus; ALT=Alanine aminotransferase

Table 2: Summaries of virological responses, discontinuation rate, and dose modification of chronic hepatitis C patients

Variables	Total (*n*=314)	Age group (years)			*P**
		<40	40-59	≥60	
RVR (ITT)	169 (53.8)	78/121 (64.5)	76/145 (52.4)	15/48 (31.3)	<0.001
RVR (PP)	124 (46.3)	56/97 (57.7)	58/131 (44.3)	10/40 (25.0)	0.002
EVR (ITT)	164 (52.2)	71/121 (58.7)	74/145 (51.0)	19/48 (39.6)	0.075
EVR (PP)	126 (47.0)	54/97 (55.7)	59/131 (45.0)	13/40 (32.5)	0.039
ETR (ITT)	183 (58.3)	74/121 (61.2)	87/145 (60.0)	22/48 (45.8)	0.161
ETR (PP)	151 (55.9)	63/97 (63.6)	71/131 (54.2)	17/40 (55.9)	0.065
SVR (ITT)	162 (51.6)	70/121 (57.9)	75/145 (51.7)	17/48 (35.4)	0.031
SVR (PP)	162 (60.4)	70/97 (72.2)	75/131 (57.3)	17/40 (42.5)	0.003
Discontinuation rate	44 (14.0)	15/121 (12.4)	15/145 (10.3)	14/48 (29.2)	0.004
Loss to follow-up	33 (10.5)	11/121 (9.1)	16/145 (11.0)	5/48 (12.5)	0.777
Dose reduction	33 (10.5)	11/121 (9.1)	14/145 (9.7)	8/48 (16.7)	0.316
Peginterferon	24 (7.6)	6/121 (5.0)	12/145 (8.3)	6/48 (12.5)	0.232
Ribavirin	12 (3.8)	6/121 (5.0)	4/145 (2.8)	2/48 (4.2)	0.665

*Comparison among age groups. RVR=Rapid virological response; EVR=Early virological response; ETR=End of treatment virological response; SVR=Sustained virological response; ITT=Intention-to-treat; PP=Per protocol

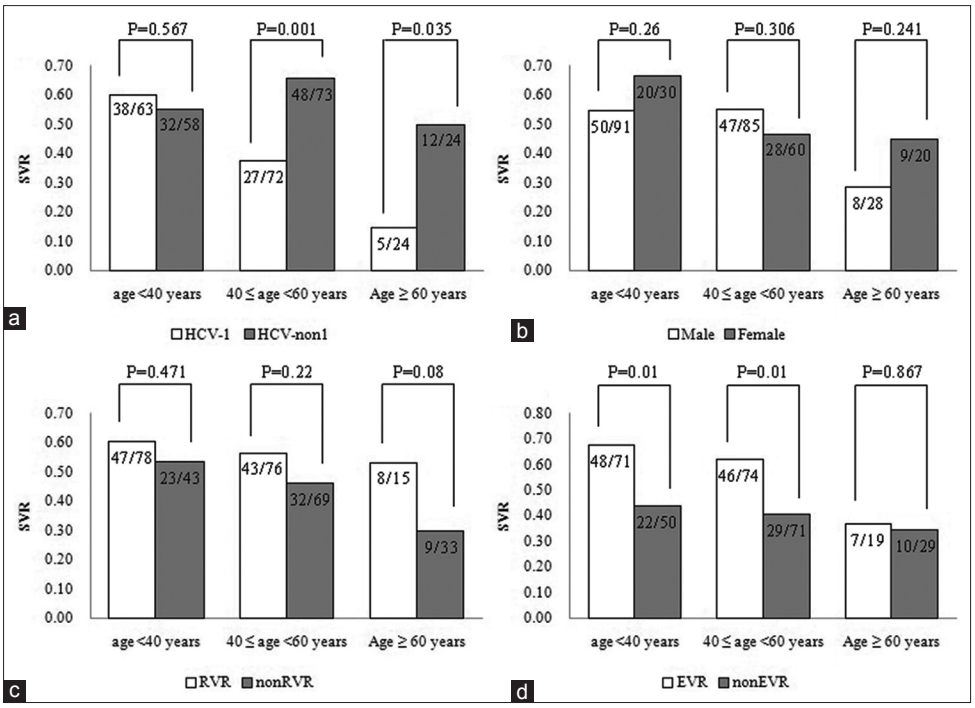

Figure 1: Sustained virological response according to age by hepatitis C virus genotype (a), gender (b), rapid virological response (c), and early virological response (d)

Table 3: Reasons for discontinuation of therapy

Variables	Total (n=314)	Age group (years)		
		<40 (n=121)	40-59 (n=145)	≥60 (n=48)
Adverse events				
Fever	2	1	1	0
Fatigue	5	1	1	3
Appetite loss	2	1	0	1
Depression	4	3	1	0
Rash	1	1	0	0
Digestive disorder	2	0	1	1
Pulmonary infection	3	1	2	0
Laboratory abnormality				
Neutropenia	3	1	0	2
Anemia	4	1	2	1
Thrombocytopenia	3	0	2	1
Elevation of ALT	2	0	1	0
Jaundice	3	1	0	2
Thyroid dysfunction	1	1	0	0
No effect of treatment	6	3	3	0
Hepatocellular carcinoma	3	0	1	2
Gastric cancer	1	0	0	1
Total	44 (14.0)	15 (12.4)	15 (10.3)	14 (29.2)

ALT=Alanine aminotransferase

satisfied our inclusion criteria were evaluated and treated with peginterferon alfa plus ribavirin. We grouped the patients according to their age as follows: 121 (38.5%) patients were aged below 40 years, 145 (46.2%) patients were aged between 40 and 59 years, and 48 (15.3%) patients were aged 60 years and above. The median age was 46.5 years (15–76 years).

Table 1 shows the baseline characteristics of each age group. Exposure category ($P < 0.001$), diabetes ($P < 0.001$), hypertension ($P < 0.001$), alanine aminotransferase ($P = 0.001$), neutrophil count ($P = 0.001$), Hb ($P < 0.001$), platelet count ($P < 0.001$), creatinine ($P = 0.007$), and liver histology ($P < 0.001$) were significantly different across these groups.

Virological responses

The RVR rates were significantly different among the three age groups. The RVR of the patients below 40 years was 64.5%; the RVR of the patients aged between 40 and 59 years was 52.4%; and the RVR of the patients aged 60 years and above was 31.3% ($P < 0.001$). However, no difference was found in the EVR and ETR rates of the three age groups ($P = 0.075$ and $P = 0.161$, respectively). As shown in Table 2, the ITT and PP analyses detected significant differences in the SVR rates among the three groups ($P = 0.031$ and $P = 0.003$, respectively). In the ITT analysis, the SVR of the patients aged below 40 years was 57.9%; the SVR of the patients aged between 40 and 59 years was 51.7%; the SVR of the patients aged 60 years and above was 35.4%. In the PP analysis, the SVR of the patients below 40 years was 72.2%; the SVR of the patients aged between 40 and 59 years was 57.3%; the SVR of the patients aged 60 years and above was 42.5%.

We also analyzed the SVR, RVR, and EVR of the patients who are grouped on the basis of HCV genotype, gender, and treatment response [Figure 1]. Those patients with HCV genotype non-1 and were aged over 40 years achieved

Table 4: Univariable and multivariable logistic regression model of achieving an SVR in patients with chronic hepatitis C that received peginterferon alfa plus ribavirin

Variables[Δ]	Category	Univariable analysis OR (95% CI)	*P*	Multivariable analysis OR (95% CI)	*P*
Age, per each increase of 1-year		0.98 (0.965-0.996)	0.015	0.983 (0.967-1.0)	0.05
HCV genotype	HCV-1/HCV-non-1	0.637 (0.407-0.995)	0.047	0.559 (0.349-0.895)	0.015
Treatment response					
RVR	RVR/non-RVR	1.841 (1.175-2.884)	0.008	1.206 (0.719-2.024)	0.478
EVR	EVR/non-EVR	2.591 (1.639-4.096)	<0.001	2.353 (1.411-3.922)	0.001

[Δ]All baseline covariates were included in univariable analysis. Only covariates significantly associated with SVR at univariable analysis (two-sided $P<0.10$) are showed and included in the multivariable model. RVR=Rapid virological response; EVR=Early virological response; OR=Odds ratio; 95% CI=95% Confidence interval; SVR=Sustained virological response; HCV=Hepatitis C virus

higher SVR rates [$P = 0.001$ or $P = 0.035$, Figure 1a] than those CHC patients with HCV genotype 1. No difference was found among the three groups according to gender [$P = 0.26$, $P = 0.306$, and $P = 0.241$, Figure 1b]. Those patients with RVR and were aged 60 years and above could obtain a relatively higher SVR rate than those who did not achieve an RVR [$P = 0.08$, Figure 1c]. EVR was very important for patients below 60 years [$P = 0.01$, Figure 1d].

Safety evaluation

The combination therapy discontinuation rate of the patients aged 60 years and above was significantly higher than that of the younger patients [$P = 0.004$, Table 2]. Table 3 shows the side effects observed among the patients upon their discontinuation of the treatment. Upon discontinuing the treatment, elderly patients suffered from fatigue ($P = 0.005$), neutropenia ($P = 0.013$), jaundice ($P = 0.013$), hepatocellular carcinoma ($P = 0.013$), and gastric cancer ($P = 0.018$) more frequently than the patients aged below 60 years but also discontinued the treatment. Two patients aged 60 years and above developed hepatocellular carcinoma during the treatment.

Factors associated with sustained virological response

The baseline characteristics were included in both univariable and multivariable analyses to identify the possible predictors of SVR [Table 4]. In the univariable analysis, age was significantly associated with SVR to combination therapy (OR = 0.98, 95% CI = 0.965–0.996, $P = 0.015$). HCV genotype non-1 and achieving RVR or EVR during treatment were also significantly associated with higher SVR rates. All of these variables were included in a multivariable model through logistic regression. Age was significantly lower among patients with SVR than among those without SVR (OR = 0.983, 95% CI = 0.967–1.0, $P = 0.05$). The SVR rate of the patients with HCV genotype non-1 were significantly higher than that of the HCV-1 patients (OR = 0.559, 95% CI = 0.349–0.895, $P = 0.015$). As expected, an EVR could be used as a powerful positive predictor to obtain an SVR ($P = 0.001$).

Discussion

Age is an important factor that affects the treatment of chronic HCV infection.[15] Aging is also regarded as an unfavorable factor of liver disease progression, treatment outcome, and HCC development in chronic HCV infection.[16-18] Age is also a better indicator of liver disease progression than HCV infection.[19] Therefore, elderly patients with CHC are in great need of anti-viral therapy.

The addition of a protease inhibitor to the peginterferon plus ribavirin therapy (triple therapy) has been recommended in Western countries to treat CHC patients with HCV genotype 1; interferon-free combinations of direct-acting anti-virals (DAAs) are currently in clinical development.[2,3,20] However, the peginterferon plus ribavirin combination remains the first-line regimen to treat chronic HCV infection in many countries because this regimen can lower the risk of cirrhosis and hepatocellular carcinoma; this regimen can also improve the survival rate of CHC patients who yield a high SVR by eradicating HCV and by inhibiting liver fibrosis progression.[13] In addition, the data of triple therapy are mostly considered from patients younger than 60 years;[21-23] however, recommendations have yet to be established for elderly patients. In summary, the efficacy of the peginterferon plus ribavirin therapy for elderly patients must be ensured.

The ITT and PP analyses indicated that those patients aged 60 years and above exhibited significantly lower RVR and SVR. HCV should be eradicated in the early stages of the therapeutic resolution of CHC, and RVR remains the most effective on-treatment–response predictor of SVR. Although the EVR and ETR rates were relatively higher among patients aged below 60 years than among elderly patients, no statistical difference was observed between these age groups. Previous studies revealed that the absence of EVR is one of the most useful and robust indicators to identify nonresponders. Approximately 97%–100% of treatment-naive patients with HCV genotype 1 infection and no EVR also failed to achieve an SVR.[1,2,24] ETR cannot accurately predict the occurrence of SVR but is necessary

to permit this occurrence. The sub-group analysis showed that elderly patients with an RVR may have a high chance to achieve an SVR; furthermore, younger patients should achieve an EVR to achieve an SVR. Thus, the treatment–response guide regimen should be assessed on an individual basis.

The occurrences of therapy discontinuation and dose reduction in the sample were 14.0% and 10.5%, respectively, which were lower than those reported in previous studies.[25,26] Unlike previous studies, all of the patients in our analysis orally received leucogen tablets at the beginning of the combination therapy to prevent drug-induced neutropenia, anemia, and/or thrombocytopenia. These conditions may account for the lower dose reductions. Elderly patients demonstrated a significantly higher discontinuation rate than younger patients. Therefore, higher age is assumed as the primary driver of poor adherence to the combination therapy. Previous studies showed that the cardiovascular and pulmonary functions of patients decreased along with age, thereby reducing their resistance to ribavirin-induced anemia. The impaired renal function of elderly patients also increased their ribavirin blood levels, which could increase the frequency of adverse events.[27] Peginterferon-related adverse events, such as fatigue, fever, headache, depression, and laboratory abnormalities, were identified as the major drivers for elderly patients to decline or stop the therapy.[28] Although no differences were found in the drug dose modifications of all patients, elderly patients suffered from fatigue and neutropenia more frequently. Unfortunately, a higher percentage of elderly patients developed jaundice and malignant cancers. Since cirrhosis and ribavirin-associated hemolysis from renal insufficiency might both contribute to jaundice development, this adverse event of combination therapy should be conducted further. Future trials should focus on clinically relevant outcomes, such as liver-related cirrhosis, hepatocellular carcinoma, mortality, and morbidity.

The multivariable analysis showed that baseline age, HCV genotype, and achievement of EVR were significantly associated with SVR. Many studies proved that the HCV genotype 1 and the absence of EVR could negatively affect the achievement of an SVR,[1-3] which was reconfirmed in our analysis. Age is also an important factor that is associated with the achievement of an SVR (OR = 0.983, 95% CI = 0.967–1.0, P = 0.05). Previous studies[29,30] also identified age as an independent factor that was associated with SVR in combination therapy. A higher rate of treatment discontinuation among elderly patients because of a higher incidence of adverse events might explain their low virological responses to the treatment. The incidence of cytopenias increased along with age, and drug dose reductions were more frequently observed among patients aged 60 years and above.[25,26,31] A significantly higher incidence of side effects, low neutrophil levels, low Hb levels, and low platelet levels were also observed among elderly patients. Other comorbid conditions, such as diabetes and hypertension, happened frequently among these patients. Diabetes was not identified in the analysis as a risk factor for SVR, but an HCV infection could induce insulin resistance, which in turn could contribute to fibrosis progression and impaired response to combination therapy.[32,33] Previous reports revealed that diabetes are associated with reduced rates of initial virological response as well as SVR in CHC patients treated with a combination of peginterferon and ribavirin.[34] In the current analysis, diabetes was significantly more frequent in elderly patients, which should be considered as a potential risk factor for their virological responses. Elderly patients also suffered from an advanced fibrosis stage, but only a small proportion of these patients had liver histology analysis. As we know, tolerance and virological response to anti-viral HCV treatment is poor in advanced fibrosis.[24,35] Previous reports also showed that liver disease could advance along with age.[36] The increase in bridging fibrosis or cirrhosis along with age was associated with a reduced sustained response to combination therapy. Therefore, cirrhosis has a higher prevalence among elderly patients.[37] All these interactions may explain the reduced efficacy of the treatment and the poorer adherence of elderly patients. A more detailed evaluation, including the baseline characteristics, major organ impairments, and comorbid conditions, is warranted.

This study has several limitations that mainly concern its retrospective design and relatively small sample of elderly patients. Regardless of potential bias, the elderly patients who are examined in this study have a high diabetes rate, high hypertension rate, low alanine aminotransferase levels, low neutrophil levels, low Hb levels, low platelet levels, and advanced fibrosis stage, which may all be associated with the outcomes of their combination therapy.

Conclusions

Elderly CHC patients with HCV genotype non-1 or who are characterized by factors that are predictive of better outcomes must undergo a peginterferon plus ribavirin combined therapy when no DAAs are available. Moreover, those patients who are infected by HCV genotype 1 must undergo treatment under careful monitoring if no obvious contraindications or major comorbidities that can compromise their lives are observed. However, the treatment has a low efficacy for elderly patients because they frequently experience adverse events and show poorer adherence to the treatment. We expect that new drugs, such as DAAs, will be used for elderly patients, including those with advanced liver disease.

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Conflicts of interest

There are no conflicts of interest.

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