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Hepatitis C Virus in the Elderly in the Direct-Acting Antiviral Era: from Diagnosis to Cure

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Abstract

Purpose of review Hepatitis C (HCV) is the most common cause of viral hepatitis in elderly individuals. This patient population previously experienced suboptimal outcomes with interferon-based regimens. Unfortunately, patients aged 65 years and older were under-represented in phase 2 and 3 clinical trials with newer direct acting antiviral (DAA) therapies. Since the advent of second-generation DAA in 2013, numerous robust real-world experiences highlighting the efficacy and safety of DAA in the elderly have been published. This review article summarizes the cascade of care for hepatitis C from diagnosis to cure from an evidence-based perspective of the aging population.

Recent finding In a large study from the Veterans Affairs Healthcare System, the overall sustained virologic response (SVR) of 15,884 patients treated with DAA regimens was 91.2%. These newer therapies remained highly effective in the subset of patients aged

65 years and older with SVR rates above 90%. A Spanish National Registry reported outcomes in patients ≥ 65 years old treated for HCV with oral DAA regimens over a 2-year period. The overall SVR was 94% in the study of 1252 subjects.

Summary Current real-world data imply DAA treatment regimens remain highly effective and safe in elderly patients when compared to the general population.

Introduction

Chronic hepatitis C affects 71 million people worldwide according to the World Health Organization (WHO) estimates [1]. WHO aims to decrease the incidence of hepatitis C by 80% and mortality by 65% globally by the year 2030. In the United States, chronic hepatitis C virus (HCV) has the highest mortality attributed to any infectious disease [2]. In 2012, the Centers for Disease Control and Prevention (CDC) added recommendations for one-time HCV screening in all persons born between 1945 and 1965, regardless of the presence or absence of HCV risk factors. [3]. This birth cohort accounted for 65% of all chronic HCV infections among adults in the United States [4]. Infection with HCV should be identified early in this aging population as older adults tend to have rapid progression of hepatic fibrosis [5–8].

Historically, elderly patients experienced suboptimal outcomes with interferon-based regimens due to poor efficacy and tolerability [9]. Newer direct-acting antivirals (DAA) are highly effective with sustained virologic response (SVR) rates above 90% [10–14]. These interferon-free treatment regimens also have improved safety profiles with the most common side effects including headache and fatigue. Unfortunately, patients aged 65 years and older were underrepresented in phase 2 and 3 clinical trials for DAA. Thus, outcomes of newer HCV therapies in this patient cohort remained uncertain. In this review, we focus on the cascade of care for HCV treatment in elderly patients, including evidence surrounding the use of DAA in persons greater than or equal to 65 years of age.

Screening

- Identification of elderly individuals infected with chronic HCV is a critical first step.

Studies have shown that 3.5% of the baby boomer birth cohort is HCV antibody positive, which is more than twice the prevalence seen in any other age cohort within the United States [15]. The initial HCV antibody test, if positive, requires another specimen for hepatitis C RNA polymerase chain reaction (PCR) as a confirmatory test. Infrequently, patients exposed to HCV can spontaneously clear the virus during the initial 6 months of the acute phase. A positive HCV antibody proves exposure whereas a positive HCV RNA confirms diagnosis of active infection. Most laboratories now offer reflex HCV RNA testing, which allows a positive antibody test to trigger an automatic RNA test from the same specimen. Automatic reflex RNA testing shortens the screening process allowing for quicker linkage to care. Table 1 lists the CDC recommendations of who should be tested for HCV.

Table 1. CDC recommendations for hepatitis C screening among adults in the United States

- Universal hepatitis C screening:
 - Hepatitis C screening at least once in a lifetime for all adults aged 18 years and older, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is less than 0.1%
 - Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is less than 0.1%
- One-time hepatitis C testing regardless of age or setting prevalence among people with recognized conditions or exposures:
 - People with HIV
 - People who ever injected drugs and shared needles, syringes, or other drug preparation equipment, including those who injected once or a few times many years ago
 - People with selected medical conditions, including:
 - people who ever received maintenance hemodialysis
 - people with persistently abnormal ALT levels
 - Prior recipients of transfusions or organ transplants, including:
 - people who received clotting factor concentrates produced before 1987
 - people who received a transfusion of blood or blood components before July 1992
 - people who received an organ transplant before July 1992
 - people who were notified that they received blood from a donor who later tested positive for HCV infection
 - Healthcare, emergency medical, and public safety personnel after needle sticks, sharps, or mucosal exposures to HCV-positive blood
 - Children born to mothers with HCV infection
- Routine periodic testing for people with ongoing risk factors, while risk factors persist:
 - People who currently inject drugs and share needles, syringes, or other drug preparation equipment
 - People with selected medical conditions, including:
 - people who ever received maintenance hemodialysis
- Any person who requests hepatitis C testing should receive it, regardless of disclosure of risk, because many persons may be reluctant to disclose stigmatizing risks

Updated recommendations by the CDC for routine screening of baby boomers, adults born between 1945 and 1965, have allowed for increased detection of disease burden in this difficult-to-treat population. Hospitals and health systems throughout the country implemented automatic age cohort HCV testing alerts in the electronic medical records which have exponentially increased HCV screening capacity [8].

Linkage to HCV care providers

- Despite accessible linkage to care in the past, innovative care models may further improve efforts for HCV eradication.

Management of hepatitis C can be challenging in the elderly population due to existing comorbidities and other aging-related factors. The availability of hepatologists may be scarce in certain communities. Innovative care models have been established throughout the country from the emergence of necessity. Project Echo started in New Mexico with the intention to expand access to liver specialists within rural areas in 2003. The interactive video platform is used to build knowledge and expertise in rural areas allowing greater access to specialists in real-time collaboration with local community providers. Project Echo effectively tele-mentors 50 programs in 39 countries spreading knowledge beyond borders [16]. Alternatively, the Veterans Affairs (VA) system, the largest hepatitis C care provider in the United States, developed an interdisciplinary model. A VA medical clinic in Indianapolis increased hepatitis C treating capacity by incorporating pharmacists. After the initial visit with an HCV clinic provider, subsequent visits were referred to the pharmacist-run HCV clinic. Utilizing three pharmacists for five half days per week allowed up to 35 additional patient appointments. The implementation of this model doubled the number of HCV patients with comparable efficacy in regards to SVR [17].

Medication access is an unavoidable hurdle in treating hepatitis C due to high medication cost and lack of insurance. Often times, the medication of choice is dependent on the patient's prescription insurance formulary unless medical necessity dictates alternative therapy. Thus, for a successful hepatitis C treatment program, traditional healthcare models should be reevaluated to maximize their capacity to screen and treat hepatitis C. Figure 1 summarizes the optimal cascade of hepatitis C care.

Treatment considerations

- Several patient-specific factors should be considered when evaluating for HCV treatment.

Prior to initiating HCV treatment, HCV genotype, treatment history, liver fibrosis, and potential concomitant drug-drug interactions must be assessed. Baseline laboratory tests, including a complete blood count and comprehensive metabolic panel along with hepatitis C genotype and HCV PCR with quantitative levels, should be checked within 6 months before initiating HCV therapy [18]. Patients who are cirrhotic need to be assessed for decompensated disease. International normalized ratio, albumin, total bilirubin, presence or absence of ascites, and hepatic encephalopathy are all components of the Child-Turcotte-Pugh score required to evaluate the state of cirrhosis.

Screening for hepatitis B virus (HBV) is also a prerequisite to HCV treatment. HBV core total antibody, HBV surface antigen (HBsAg), and HBV surface antibody should be assessed to evaluate the risk of HBV reactivation. There are two different approaches to HBsAg positive patients with low or undetectable HBV DNA. The conservative option is to initiate HBV treatment a week before starting HCV treatment. HBV treatment should be continued until 12 weeks after completing HCV therapy. The alternative option is to monitor monthly for HBV infection during and immediately after HCV treatment. If this pre-emptive strategy is utilized, HBV treatment should be initiated if there is a

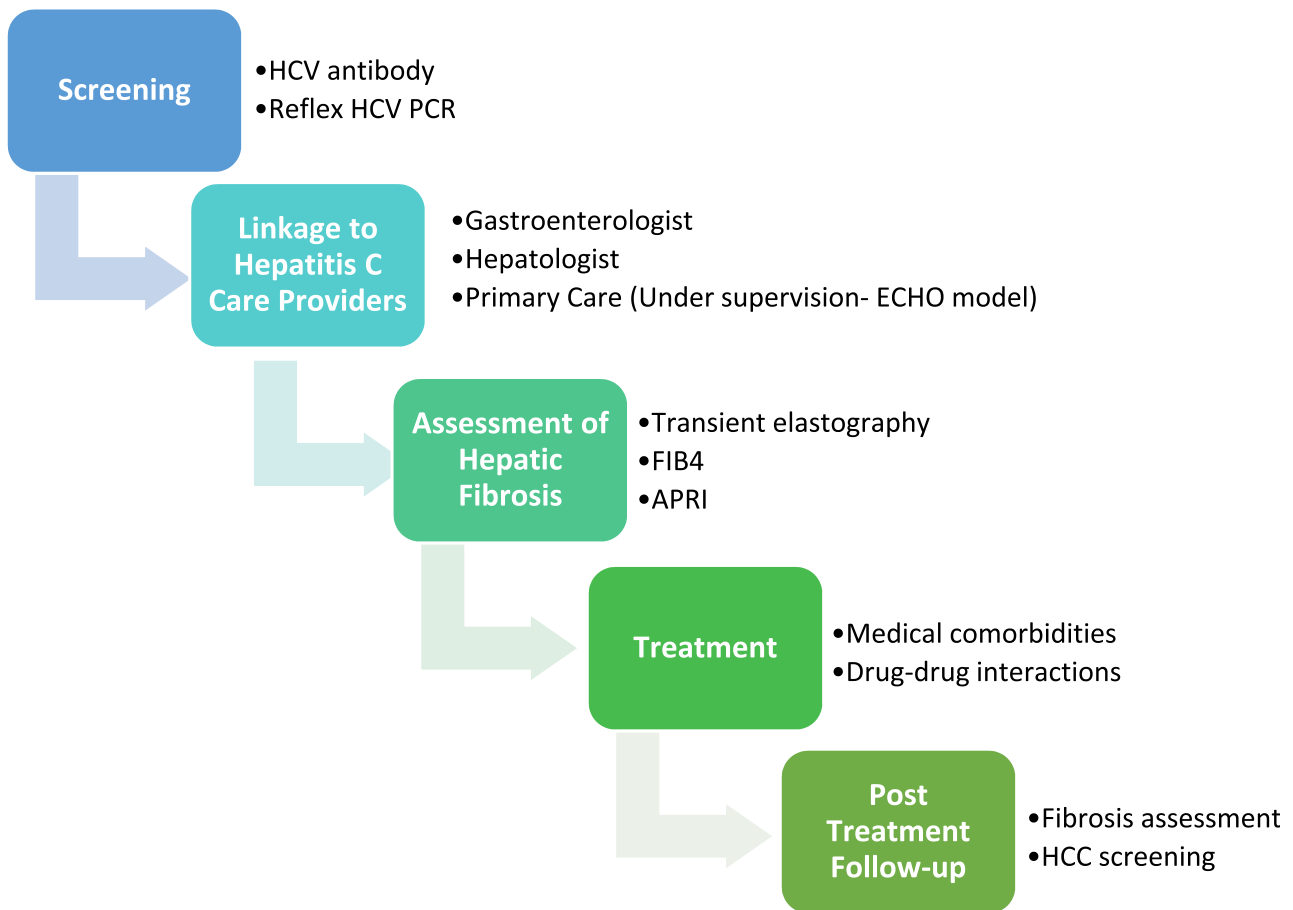


Fig. 1. Cascade of linkage to care in elderly with hepatitis C virus

significant rise in HBV DNA levels.

Given the complex medical comorbidities in the elderly, coupled with their cumulative progression to cirrhosis and hepatocellular carcinoma, early referral to providers with experience in the management of HCV is essential [19–21]. Baseline hepatic fibrosis should be assessed with non-invasive modalities including transient electrography (FibroScan®) or more accessible indices such as a calculated Fibrosis-4 (FIB-4) score, aminotransferase to platelet ratio index (APRI), or the FibroSure® blood test [18].

Older adults with concomitant medications due to other underlying chronic comorbidities such as renal failure or cardiovascular disease should have a thorough drug-drug interaction analysis with potential HCV regimens. Therefore, an interdisciplinary team approach is paramount to the safety and success of curing HCV.

Pharmacologic treatments

In clinical practice, there are currently five HCV DAA therapies available. Three of these regimens are pangenotypic, including glecaprevir/pibrentasvir,

sofosbuvir/velpatasvir, and sofosbuvir/velpatasvir/voxilaprevir. Treatment duration usually spans 8–12 weeks, but may extend up to 16–24 weeks depending on HCV genotype, stage of fibrosis, and treatment history.

There are three classes of direct acting antivirals used to disrupt the HCV life cycle. The NS3/4A protease inhibitors end with the suffix “-previr”, the NS5A inhibitors end with the suffix “-asvir”, and the NS5B polymerase inhibitors (both nucleoside and nonnucleoside analogs) end with the suffix “-buvir”.

Ledipasvir/sofosbuvir

Ledipasvir/sofosbuvir is indicated for HCV genotypes 1, 4, 5, and 6. Weight-based ribavirin dosing should be added to this combination in patients with decompensated cirrhosis and in liver transplant recipients with compensated cirrhosis. This treatment regimen can be shortened to 8 weeks in patients infected with HCV genotype 1 who are treatment-naïve, noncirrhotic, and have a pretreatment HCV RNA less than 6 million IU/ml.

Elbasvir/grazoprevir

Elbasvir/grazoprevir can be used to treat HCV genotypes 1 and 4 for a recommended treatment duration of 12 weeks. Resistance testing is required prior to use in patients with genotype 1a. Grazoprevir is a protease inhibitor; therefore, this combination therapy should not be used in patients with decompensated cirrhosis.

Glecaprevir/pibrentasvir

Glecaprevir/pibrentasvir is a pangenotypic regimen that may be used to treat HCV genotypes 1–6. This combination is administered as three tablets once daily, which differs from other single tablet DAA regimens. On the other hand, glecaprevir/pibrentasvir has a shorter recommended duration of 8 weeks for patients who are treatment naïve, with or without compensated cirrhosis, regardless of genotype. This combination can also be used in patients who have previously failed treatment with DAA therapies. Glecaprevir is a protease inhibitor; therefore, this combination therapy should not be used in patients with decompensated cirrhosis.

Sofosbuvir/velpatasvir.

Sofosbuvir/velpatasvir is a 12-week pangenotypic treatment regimen. This combination is an important option for the hard-to-treat genotype 3-infected patients with decompensated cirrhosis. The addition of weight-based ribavirin is recommended in any patient with decompensated cirrhosis.

Sofosbuvir/velpatasvir/voxilaprevir

Sofosbuvir/velpatasvir/voxilaprevir, a pangenotypic combination therapy, is reserved for use as a 12-week treatment in patients who previously failed DAA regimens. This combination is also an option for patients infected with HCV

genotype 3 who have compensated cirrhosis and have previously failed treatment with peginterferon/ribavirin.

Benefits of therapy

As the HCV population grows older, there will be an expected increase in liver-related complications including cirrhosis and hepatocellular carcinoma [20]. Achievement of HCV eradication will avoid significant healthcare costs caused by the burden of disease [22]. Additionally, there is evidence demonstrating an association between chronic HCV infection with metabolic disorders, fatigue, depression, and poor quality of life [23–25]. Achieving HCV cure has been shown to improve these extra-hepatic complications [22, 26]. Current literature also suggests that anti-HCV treatment may reduce the risk of end-stage renal disease, coronary artery disease, and cerebrovascular accidents [24, 26].

Evidence from phase 2 and phase 3 clinical trials

Saab and colleagues compared outcomes in patients < 65 years old to those ≥ 65 years old who received HCV treatment with ledipasvir/sofosbuvir with or without weight-based ribavirin for 8, 12, or 24 weeks [27]. The authors pooled data from four phase 3 clinical trials. The study included 264 patients aged 65 years or older, with 20% having compensated cirrhosis. The authors found similar rates of sustained virologic response at 12 weeks after completion of therapy (SVR12) between patients < 65 years old and those ≥ 65 years old (97% vs. 98%, respectively). Efficacy remained high among patients 75 years or older, with 100% achieving SVR12. Tolerability was similar between groups, with 78% of patients < 65 years old and 80% of patients ≥ 65 years old reporting adverse effects, the most common being headache and fatigue. This study reported a higher rate of study drug modification or interruption among patients treated with ribavirin in both age groups, with the elderly experiencing a higher incidence (6% < 65 years vs. 13% ≥ 65 years).

In a study conducted by Foster and colleagues, data was combined from nine phase 2 and phase 3 clinical trials to evaluate efficacy and safety outcomes in HCV patients ≥ 65 years old treated with the pan-genotypic regimen, glecaprevir/pibrentasvir, for 8, 12, or 16 weeks [28]. Overall, the authors included 2369 subjects with 328 subjects ≥ 65 years old, including 47 patients aged 75 years or older. Of the elderly individuals, 20% had cirrhosis at baseline. SVR12 rates were similar between groups (97.3% in < 65 and 97.9% in ≥ 65 years old). Rates of adverse effects and discontinuation due to DAA-related adverse effects were also similar between groups.

Shiffman and colleagues reported outcomes of 123 patients aged 65 years or older enrolled in three phase 3 studies who received sofosbuvir/velpatasvir, a pan-genotypic DAA, for 12 weeks for the treatment of chronic HCV [29]. Fourteen of the patients were ≥ 75 years old. All of the elderly patients achieved SVR12 compared to 97.8% of the younger subjects. Similar to other DAAs, the most commonly reported side effects were headache, fatigue, nausea, and nasopharyngitis. None

of the older patients required treatment discontinuation due to adverse effects.

Flamm et al. conducted an integrated retrospective analysis to evaluate the safety and efficacy of elbasvir/grazoprevir in the elderly population [30]. They pooled data from twelve phase 2 and 3 trials comprising 2478 subjects with HCV genotype 1 or 4. Three hundred and thirty-nine patients were ≥ 65 years old, with 19% being cirrhotic. After 12 weeks of treatment, sustained virologic cure rates were similar between groups in the intent-to-treat population (95.4% < 65 years vs. 95.3% ≥ 65 years). Serious adverse drug effects and discontinuations due to adverse effects were rare in both groups.

Real-world experience

A large Veterans Affairs Healthcare System retrospective study utilized data from patients who completed HCV DAA therapies over a 27-month period [31••]. DAA treatments included sofosbuvir-based, and paritaprevir/ritonavir/ombitasvir plus dasabuvir-based regimens. Among the 15,884 patients with SVR data, the overall SVR was 91.2%. The percentage of patients over the age of 65 years was 27.8%. SVR rates were comparable in the elderly age cohorts: 91.1% in patients between 65 and 69 years, 90% in patients 70–74 years, and 93.8% in patients ≥ 75 years of age.

A multicenter observation study utilizing data from the Spanish National Registry reported outcomes in patients aged 65 years and older who were treated for HCV with oral DAA regimens over a two-year time period [32••]. Of the 1252 subjects, 76% were 65–74 years of age, 17% were 75–79 years of age, 7% were 80 years or older, and 74% of all patients had cirrhosis. Overall, 33.3% took ledipasvir/sofosbuvir with or without ribavirin, 28% paritaprevir/ritonavir/ombitasvir plus dasabuvir with or without ribavirin, and 26% received sofosbuvir plus simeprevir with or without ribavirin. The remaining subjects received other oral DAA regimens. The overall SVR12 rate in the intent-to-treat population was 94%. There was no significant difference in SVR rates among age groups, but there was an increase in serious adverse effects among patients 75 years or older (8.8% in 65–74 years, 13% in 75–79 years, and 14% in ≥ 80 years).

In a retrospective cohort study conducted by Conti and colleagues, 556 patients (50.7% ≥ 65 years old) were treated for HCV infection with DAA regimens at 11 centers in Italy [33•]. More patients in the elderly group were cirrhotic (86.5% vs. 78.1% in the < 65 group, $P = 0.010$). SVR12 rates were similar between age groups (90.5% in < 65 years vs. 94.7% in ≥ 65 years, $P = 0.074$). Advanced fibrosis and cirrhosis did not hinder efficacy outcomes, but the severity of liver disease did affect SVR12 rates (95.5% in Child-Turcotte-Pugh A vs. 90.8% in Child-Turcotte-Pugh B, $P = 0.010$). More patients in the elderly group reported adverse effects (54.6% in elderly vs. 38.7% in < 65 years group); however, the rates of serious adverse effects and discontinuation of therapy were similar between groups.

Two meta-analyses reviewed clinical trials and post-marketing studies to evaluate the efficacy and safety of DAA regimens in the elderly population [34, 35]. Overall, DAA therapies are highly effective and well-tolerated in patients ≥ 65 years old. Both studies also found that older patients treated with

ribavirin are at an increased risk of developing anemia.

There are currently no recommendations for an upper age limit for patients requiring HCV treatment [18]. Current literature suggests that DAA regimens are safe and effective for the treatment of HCV in the elderly population; however, the addition of ribavirin should be avoided if possible due to the risk of adverse effects.

Comorbidities and drug-drug interactions

Elderly patients have a higher prevalence of comorbidities, including cirrhosis, hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, and chronic kidney disease [28, 30, 31••, 32••, 33•]. When compared to the younger population, patients ≥ 65 years old are also more likely to have lower albumin and hemoglobin levels at baseline. It does not appear that these comorbidities have an effect on treatment response; however, comorbid medical conditions should be considered when assessing the life expectancy of the patient.

Given their higher number of comorbidities, patients ≥ 65 years old generally require an increased number of medications [28, 30, 32••, 36]. Prescribers and pharmacists should evaluate concomitant medications for potential drug-drug interactions when selecting DAA regimens. One study compared possible drug-drug interactions between patients < 65 years and patients ≥ 65 years treated with various DAA regimens [36]. There were 404 patients in the < 65 years group and 137 in the elderly group. There was a total of 152 different medications taken concomitantly with DAA therapy, with the most common being proton pump inhibitors, beta-blockers, thyroid medications, loop diuretics, angiotensin-converting enzyme inhibitors, vitamin D supplements, and insulins. More patients in the ≥ 65 years group were taking concomitant medication therapies compared to the younger group (79% vs. 51%, respectively, $P < 0.0001$), with 35% of patients ≥ 65 years requiring at least four medications. There was a higher rate of clinically significant drug-drug interactions predicted in the elderly group (54% vs. 28% in the < 65 years, $P < 0.0001$). Interactions were determined to be clinically significant if they required close monitoring, dose modifications, changes in administration times, or if co-administration was not recommended or contraindicated.

Comprehensive drug-drug interaction databases are encouraged if practitioners are uncertain of interactions between DAA regimens and concomitant medication therapies. Table 2 provides an overview of common drug-drug interactions with currently available DAA regimens. Practitioners should also address pharmacodynamic interactions, including the risk of hypoglycemia with anti-diabetic medications and more frequent monitoring of warfarin therapies due to changes in hepatic function throughout DAA treatment.

Clinical monitoring

Laboratory testing may be monitored at treatment week 4, the end of treatment, and 12 weeks after the treatment has been completed. The comprehensive metabolic panel and quantitative HCV RNA PCR should be reviewed at each time point. In cirrhotic patients, particularly those with decompensation

Table 2. Drug-drug interactions with commonly prescribed medications in patients with chronic HCV infection. The color scheme represents the level of clinical significance according to the hep-druginteractions.org website: green = no interaction; yellow = weak interaction; orange = potential interaction; red = strong interaction/contraindicated

Medication Class	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/ Velpatasvir/ Voxilaprevir
PPI	Give concurrently; do not exceed PPI 20 mg daily	No interaction	Do not exceed PPI 40 mg daily	If medically necessary, give PPI 4 hours after; do not exceed PPI 20 mg daily	If medically necessary, give concurrently; do not exceed PPI 20 mg daily
H2RA	Give H2RA concurrently or 12 hours apart; do not exceed 40 mg twice daily	No interaction	No clinically significant reduction in GP exposure	Give H2RA concurrently or 12 hours apart; do not exceed 40 mg twice daily	Give H2RA concurrently; do not exceed 40 mg twice daily
Antacids	Separate by 4 hours	No interaction	No interaction	Separate by 4 hours	Separate by 4 hours
Anti-Hypertensives /Anti-Arrhythmics	↑Carvedilol	No interactions with carvedilol or diltiazem	↑Carvedilol ↑Diltiazem ↑Amiodarone	↑Carvedilol ↑Diltiazem	↑Carvedilol ↑Diltiazem
	Do not give with amiodarone	↑Amiodarone		Do not give with amiodarone	Do not give with amiodarone
Lipid Lowering Agents	Do not administer with ROS	↑ATO, ROS, LOV, SIM	Do not administer with ATO, LOV, SIM	↑ATO, ROS, LOV, SIM	Do not administer with ATO, ROS, LOV, SIM
	↑ATO, LOV, SIM, PRA	No interaction with PRA	↑ROS, PRA	No interaction with PRA	↑PRA
Diabetic Medications	No interaction	No interaction	No interaction	No interaction	No interaction
Levothyroxine	No interaction	No interaction	No interaction	No interaction	No interaction

PPI proton pump inhibitors, omeprazole equivalent, H2RA histamine 2 receptor antagonists, famotidine equivalent, ATO atorvastatin, ROS rosuvastatin, LOV lovastatin, SIM simvastatin, PRA pravastatin, "↑" = increased exposure, "↓" = decreased exposure

requiring treatment with ribavirin, a complete blood count should also be collected. It is recommended to monitor patients with decompensated cirrhosis more frequently than the aforementioned schedule. The quantitative HCV RNA PCR should have a detection level of < 25 IU/ml to be deemed “undetectable.” This number may differ depending on the laboratory-specific calibration. Hepatitis C virologic cure can be concluded with an undetectable HCV RNA 12 weeks after HCV treatment completion.

Resistance testing

HCV resistance most commonly occurs when the virus is exposed to sub-therapeutic concentrations of the drug. Transmission of an HCV strain with preexisting resistance may also occur despite the patient lacking previous exposure to hepatitis C therapy. The clinically impactful resistance-associated-substitutions (RAS) mostly develop against NS5A inhibitors and NS3/4A protease inhibitor-containing regimens. RAS against NS5A inhibitors can persist for years and are more fit than others with Y93H being the most prevalent RAS across genotypes [18].

The American Association for the Study of Liver Diseases recommends baseline testing for NS5A RAS in genotype-specific cohorts. Genotype 3 treatment-naïve patients with cirrhosis and treatment-experienced patients with or without cirrhosis, in whom sofosbuvir/velpatasvir is being evaluated, should receive NS5A RAS testing at baseline. If Y93H is present, weight-based ribavirin should be added or a different treatment regimen should be prescribed. With respect to ledipasvir/sofosbuvir, baseline resistance testing should be considered in those infected with genotype 1a who are treatment-experienced with or without cirrhosis. If Y93H is present, a different treatment regimen should be prescribed. Lastly, baseline resistance testing is recommended in all genotype 1a patients, including both treatment-naïve and treatment-experienced, for whom elbasvir/grazoprevir is being considered and a different regimen should be prescribed if Y93H is present [18]. In summary, the specific genotype and presence of NS5A RAS with certain treatment regimens may result in exponentially higher drug resistance, ultimately impacting SVR.

Post hepatitis C treatment follow-up

Retrospective studies have shown regression in fibrosis after treatment of the original liver disease, including chronic HCV eradication [37–40]. Pre-treatment hepatic fibrosis staging by noninvasive methods can be compared against testing after the achievement of SVR to assess for clinical response [41]. Despite the cure of HCV, elderly patients remain at increased risk of liver-related complications, including advanced fibrosis and hepatocellular carcinoma, likely due to other concomitant comorbidities such as non-alcoholic steatohepatitis and other metabolic syndromes [42, 43]. Older age is also associated with an increased risk of hepatocellular carcinoma without evidence of significant hepatic fibrosis after eradication of HCV [44, 45]. Prescribers should maintain ongoing care for older adults with significant pre-treatment hepatic fibrosis. In these patients, routine surveillance imaging for hepatocellular

carcinoma should be continued even after achieving HCV cure. Patients with cirrhosis should be monitored every 6 months.

Conclusion

Elderly patients share the highest burden of chronic HCV worldwide with liver-related complications, including advanced fibrosis and hepatocellular carcinoma, being more common among older adults. Screening and treatment of chronic HCV in this patient population will facilitate the goal of HCV eradication by 2030. Albeit previous experience with interferon-based therapies may have hindered HCV treatment in the elderly, current DAA treatment regimens appear to be generally safe and highly effective in patients ≥ 65 years old. Healthcare practitioners should continue to ambitiously work towards achieving HCV eradication by screening and safely treating the elderly population.

Compliance with Ethical Standards

Conflict of Interest

Dr. Satapathy reports grants from Gilead Sciences, grants from Conatus Pharma, grants and other from Intercept Pharma, other from Alexion, grants from Genfit, grants and other from Dova, grants and other from Bayer, grants from Exact Sciences, grants and other from Biotest, grants from Shire NASH, grants from Enanta, outside the submitted work. The other authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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