Making a Decision on When to Initiate HCV Therapy

This is a PDF version of the following document:
Section 4: Evaluation and Preparation for Hepatitis C Treatment
Topic 2: Making a Decision on When to Initiate HCV Therapy

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Indications for Treatment

Background

Multiple studies have shown that successful antiviral therapy of chronic hepatitis C virus (HCV) infection dramatically reduces both liver-related morbidity (including rates of end-stage liver disease and hepatocellular carcinoma) and mortality, as well as all-cause mortality.[1,2,3,4] Direct-acting antiviral (DAA) treatment for HCV has proven to be much safer, better tolerated, and more effective than treatments used in the interferon era, now rendering the decision to initiate therapy much easier. The cooperative guidance issued from the American Association for the Study of Liver Disease and Infectious Diseases Society of America (AASLD-IDSA) notes that evidence clearly supports treatment of nearly all persons with chronic HCV infection.[5] Decisions regarding initiating therapy will naturally be influenced by the patient's willingness and readiness to undertake treatment.

Generally Accepted Indicators for Treatment

The AASLD-IDSA guidance previously provided a priority ranking for treatment based on clinical factors and public health considerations.[5] These priority ranking arose, in part, due to the relatively limited infrastructure capable of treating the surge of persons with chronic HCV infection who had been waiting to receive treatment with new DAA therapy.[5] These treatment priority rankings are no longer used by the AASLD-IDSA guidance; instead, the current guidance emphasizes that all patients, except for those with a short (i.e. less than 1 year) life expectancy, should receive treatment for chronic HCV infection.[5] The recommendation to treat virtually all persons with chronic HCV infection stems from multiple factors, including the very high sustained virologic response (SVR) rates with DAA therapy, the safety and tolerability of DAA therapy, and the preponderance of data demonstrating benefit across a spectrum of clinical outcomes with achievement of SVR.[5,6] The AASLD-IDSA guidance also addresses some unique populations that may require special considerations when weighing treatment decisions:[5]

- Persons with HCV and HIV coinfection
- Persons with decompensated cirrhosis
- Persons who develop HCV post liver transplantation
- Persons with renal impairment
- Persons post renal transplantation
- Management of acute HIV infection
- Pregnant women
- Children

Contraindications for Treatment

Absolute Contraindications

In the interferon-free era, even patients with decompensated cirrhosis or renal failure can undergo treatment if managed by a provider with expertise in the management of HCV in these complicated patient populations.[7,8,9] The AASLD/IDSA hepatitis C treatment guidance recommends against treating persons with short life expectancies.[5] Available data from animal studies indicate that ribavirin has significant teratogenic and embryocidal adverse effects.[10] Accordingly, use of ribavirin is contraindicated in women who are pregnant, women who may become pregnant, or men whose female partners are pregnant.[11,12] Patients with chronic hepatitis C who are of reproductive age and are to receive a regimen that includes ribavirin should be advised to use two forms of contraception during treatment and for at least 6 months following the end of treatment.[13] The AASLD-IDSA Hepatitis C guidance states that recent or active drug use is not an absolute contraindication to HCV treatment.[5] Indeed, multiple studies involving persons with past or current injection drug use have shown very good adherence and excellent SVR rates with HCV DAA therapy.[14,15,16,17] Similarly, the AASLD-IDSA guidance does not require abstinence from alcohol as a pretreatment requirement.[5]

Relative Contraindications

In addition to some absolute contraindications, there are several situations in which the clinician should exert careful consideration before starting hepatitis C treatment: active severe substance use disorder that would interfere with making follow-up appointments, psychiatric issues not optimally controlled, and social issues that may negatively impact a patient’s ability to adhere with therapy, to make visits to monitor treatment safety, or to show up for scheduled office visits.[18,19]

Patient Readiness

Assessing Readiness

A patient’s readiness to start therapy can be difficult to assess, but a checklist can be used as a general guide (Figure 1). It is important to have a frank discussion with each patient about the chance of cure, the potential side effects of therapy, the cost of treatment, and, if using a regimen that includes ribavirin, the impact of treatment on their quality of life.

Pretreatment Counseling

In addition, the HCV pretreatment discussion should cover counseling on adherence, drug interactions, potential side effects, contact numbers for after-hour questions or issues, and specific information on follow-up visits. Given the high cost of DAAs and the potential for drug resistance, it is very important that patients fully understand the importance of remaining 100% adherent with the treatment regimen.

Timing of Initiation of Treatment

The availability of DAAs has provided tremendous opportunities for highly effective, convenient, well-tolerated therapy. The high cost of these medications has created difficulty in payment and reimbursement in many regions—see Module 4, Lesson 3 (Cost and Access to Direct-Acting Antiviral Agents). These cost issues have, with some payers, forced an approach whereby those likely to receive the most immediate benefit, such as those with advanced fibrosis, are prioritized to receive therapy first. There are, however, some data that deferral of treatment until advanced stages of liver disease is a suboptimal and short-sighted approach to care.[20,21] More recently, cost of DAA therapy has significantly decreased. Nevertheless, the projected cost of widespread DAA therapy for all persons living with HCV infection in the United States may not be affordable or feasible.

Advanced Age and Comorbid Conditions

Many persons living with chronic HCV infection in the United States North American are older than age 50. With the availability of new highly effective, safe, well-tolerated regimens, it is likely that more interest and experience will accumulate in treating patients with advanced age. Notably, some clinical trials with newer direct acting antivirals have enrolled patients older than 70, but overall relatively little experience exists with treatment of HCV in patients older than 70. In some circumstances, patients may have advanced age and minimal HCV-related fibrosis and thus HCV may not be expected to play a major role in shortening their lifespan. In addition, some patients may have limited life expectancy due to other comorbid conditions, and as such, hepatitis C treatment would not be expected to alter their quality of life or life expectancy. Thus, in some situations involving patients with advanced age or significant medical comorbidities associated with expected short lifespan (less than 12 months), it may be sensible to withhold therapy.

Obtaining Authorization and Payment for Medications

If a patient has been deemed to be an appropriate candidate for antiviral therapy and is in need of therapy, the medical provider should begin investigating payment for the treatment. Because these antiviral agents are quite costly, they typically need to be preapproved. The authorization process may last several months, with the exact time dependent on the insurance coverage and state of residence. Restrictions vary by state and insurer as to who can prescribe DAAs, as well as the level of fibrosis and sobriety. In addition, individuals with HCV waiting to start treatment should be warned in advance that the DAA medication approval process may be drawn out.

Monitoring and Follow-Up if Not Treated

General Recommendations for Monitoring and Follow-Up

There may be a variety of reasons that treatment of HCV is deferred, including patient-specific barriers such as active psychosocial instability, a competing severe illness, or insurance denial. At least annual follow-up is recommended for these patients. During these visits, patients should have counseling regarding behaviors that will optimize liver health. This includes avoiding a diet high in saturated fat, achieving an optimal body weight, limiting intake of hepatotoxic medications and abstaining from or limiting alcohol intake. Medical providers should have awareness of indicators associated with accelerated hepatic fibrosis progression, such as older age at the time of HCV infection, male sex, alcohol consumption, nonalcoholic steatohepatitis (NASH), genotype 3 HCV, and coinfection with hepatitis B or HIV (Figure 2).[22,23,24] Individuals who have indicators associated with accelerated hepatic fibrosis should receive counseling regarding the risk and impact of accelerated hepatic fibrosis progression; in this setting, clinicians should attempt to promptly initiate HCV treatment. In addition, these patients should receive information and education on the warning signs and symptoms of liver dysfunction, including jaundice, melena, clay-colored stools, confusion, abdominal distention and lower extremity edema.[25,26]

Reassessing Hepatic Fibrosis

For patients with mild to moderate fibrosis (F0 to F2), fibrosis progression can occur, so it is recommended that at least a liver function panel that includes an aspartate aminotransferase (AST) and complete blood cell count with platelet count be performed annually; from these basic laboratory tests, an AST to Platelet Ratio Index (APRI) can be calculated.[27,28] In addition, subsequent noninvasive testing to reevaluate hepatic fibrosis (e.g. with a FibroSure, Fibrotest-Actitest, or transient elastography) is recommended.[29,30] The optimal interval for reevaluating hepatic fibrosis may depend on clinical factors and patient's initial stage of disease. The AASLD-IDSA guidance recommends an annual update of lab markers of hepatic function and re-evaluation interval of no greater than 6 months for patients with cirrhosis for liver cancer screening.[5]

Monitoring and Assistance with Unstable Psychosocial Situation

Individuals living chronic HCV infection who have an unstable psychosocial situation should have their issues addressed and be referred to appropriate resources, such as a mental health professional or a substance use disorder counselor. Ongoing alcohol abuse is perhaps the most worrisome behavior, because it can accelerate fibrosis and patients should be counseled strongly to abstain completely.[29,31] Special effort should be made to address psychosocial issues in patients with advanced fibrosis (F3 or F4). These patients with advanced fibrosis will also need hepatocellular carcinoma surveillance with a hepatic ultrasound, with or without alfa-fetoprotein every 6 months.[32,33]

Summary Points

- Availability of highly effective, convenient, safe, well-tolerated therapy has changed the landscape for the treatment of hepatitis C.
- Nearly all patients with hepatitis C may benefit from therapy. Those patients with a severely limited lifespan (less than 12 months) are the exception.
- The decision and timing for starting HCV therapy needs to be individualized.
- In situations when treatment is deferred (for whatever reason), the patient should periodically undergo reevaluation for disease progression and reconsideration of treatment, with the frequency of reevaluation individualized based on the patient's current fibrosis stage, likely fibrosis progression rate, and other factors that may influence treatment readiness.

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Figures

Figure 1 Patient Checklist Prior to Initiating Hepatitis C Therapy

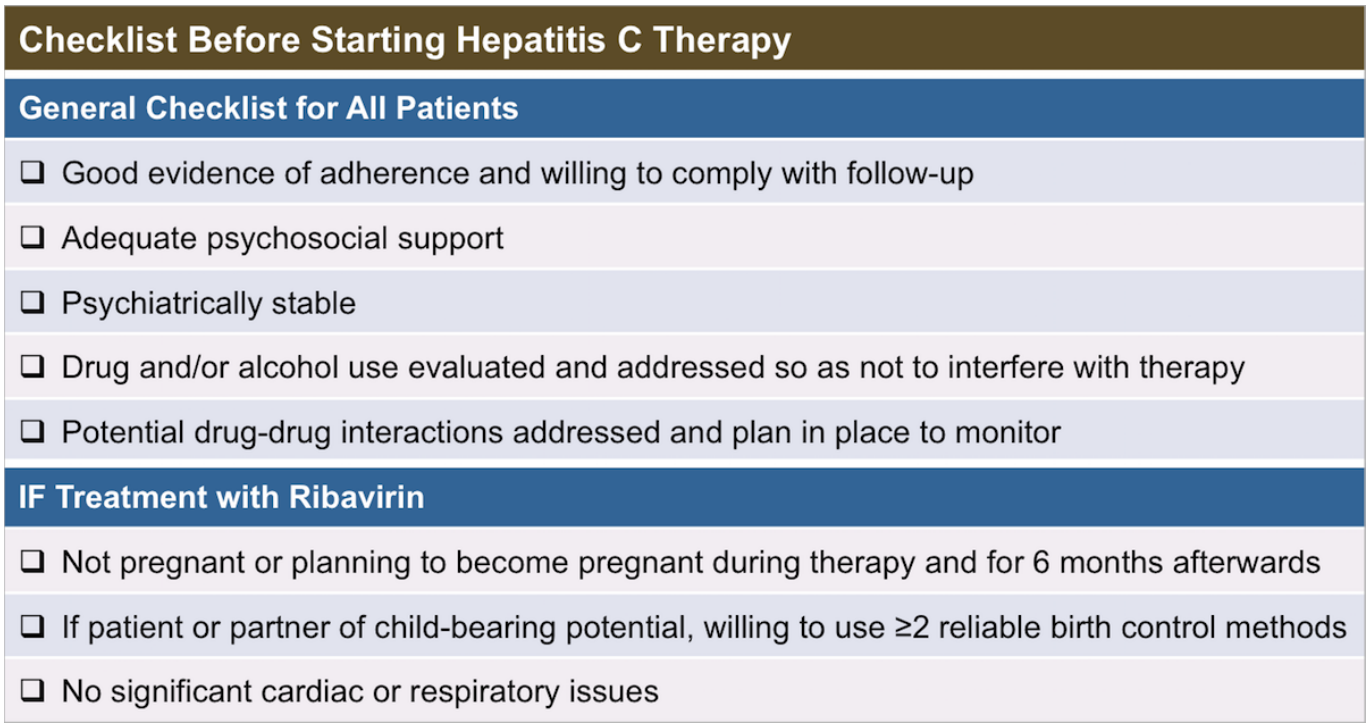

Figure 2 Factors Associated with Accelerated Fibrosis

Source: American Association for the Study of Liver Disease, the Infectious Diseases Society of America. When and in whom to initiate HCV therapy. Recommendations for testing, management, and treating hepatitis C.