Cost Effectiveness of Pre– vs Post–Liver Transplant Hepatitis C Treatment With Direct-Acting Antivirals

Sumeyye Samur,[*,‡] Brian Kues,[§] Turgay Ayer,[§] Mark S. Roberts,[‖,¶] Fasiha Kanwal,[#,**] Chin Hur,[*,‡,‡‡] Drew Michael S. Donnell,[‖,¶] Raymond T. Chung,[‡,‡‡,b] and Jagpreet Chhatwal[*,‡,‡‡,b]

*Institute for Technology Assessment, ‡‡Liver Center and Gastrointestinal Division, Massachusetts General Hospital, Boston, Massachusetts; ‡Harvard Medical School, Boston, Massachusetts; §Department of Industrial and Systems Engineering, Georgia Institute of Technology, Atlanta, Georgia; ‖Department of Health Policy and Management, University of Pittsburgh Graduate School of Public Health, Pittsburgh, Pennsylvania; ¶University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; #Department of Medicine, Gastroenterology and Hepatology, Baylor College of Medicine, Houston, Texas; **Houston Veterans Affairs Health Services Research and Development Center of Excellence, Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas

BACKGROUND & AIMS: **Oral direct-acting antivirals (DAAs) for hepatitis C virus (HCV) treatment offer new hope to both pre– and post–liver transplant (LT) patients. However, whether to treat HCV patients before vs after LT is not clear because treatment can improve liver function but could reduce the chance of receiving an LT while on the waiting list. Our objective was to evaluate the cost effectiveness of pre-LT vs post-LT HCV treatment with oral DAAs in decompensated cirrhotic patients on the LT waiting list.**

METHODS: **We used a validated mathematical model that simulated a virtual trial comparing long-term clinical and cost outcomes of pre-LT vs post-LT HCV treatment with oral DAAs. Model parameters were estimated from United Network for Organ Sharing data, SOLAR-1 and 2 trials, and published studies. For each strategy, we estimated the quality-adjusted life-year, life expectancy, cost, and the incremental cost-effectiveness ratio.**

RESULTS: **For lower MELD scores, quality-adjusted life-years were higher with pre-LT HCV treatment compared with post-LT treatment. Pre-LT HCV treatment was cost saving in patients with MELD scores of 15 or less, and cost effective in patients with MELD scores of 16 to 21. In contrast, post-LT HCV treatment was cost effective in patients with MELD scores of 22 to 29 and cost saving if MELD scores were 30 or higher. Results varied by drug prices and by United Network for Organ Sharing regions.**

CONCLUSIONS: **For cirrhotic patients awaiting LT, pre-LT HCV treatment with DAAs is cost effective/saving in patients with MELD scores of 21 or lower, whereas post-LT HCV treatment is cost effective/saving in patients with MELD scores of 22 or higher.**

Keywords: Simulation Model; Sofosbuvir; Health Economics.

Hepatitis C virus (HCV) is the leading cause of hepatocellular carcinoma and the leading indication for liver transplantation (LT) in the United States and Europe.[1] Approximately 15% to 20% of patients with HCV-related cirrhosis advance to decompensated cirrhosis or hepatocellular carcinoma within 10 years.[1] For these patients, mortality rates increase to approximately 15% to 20% per year, and liver transplant becomes the only viable option for long-term survival.[2]

Historically, treatment of HCV patients with decompensated cirrhosis who were candidates for LT or who underwent LT had been challenging because of the low efficacy and tolerability of interferon-based therapies.[3] However, with the availability of oral direct-acting antivirals (DAAs), HCV treatment now can be offered with high success rates, in both the pre- and post-LT settings.[4]

[b]Authors share co-senior authorship.

Abbreviations used in this paper: DAA, oral direct-acting antiviral; HCV, hepatitis C virus; ICER, incremental cost-effectiveness ratio; LT, liver transplantation; MELD, Model for End-stage Liver Disease; QALY, quality-adjusted life year; SVR, sustained virologic response; UNOS, United Network for Organ Sharing.

Most current article

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2017.06.024

Despite the clear benefits of DAAs, the optimal timing of HCV treatment, pre-LT vs post-LT, is not clear.[2,5] There is a trade-off—pre-LT HCV treatment can improve patients' Model for End-stage Liver Disease (MELD) score and reduce mortality while on the waiting list; however, it also may delay LT by decreasing patients' priority on the waiting list. This situation has been termed "MELD limbo" or "MELD purgatory."[5] Furthermore, by eradicating HCV before transplant, some patients no longer would be eligible to receive an HCV-positive liver, which could reduce their chance of getting a transplant further. On the other hand, for some patients, not receiving pre-LT HCV treatment and waiting until LT could result in worsening of the underlying liver condition and increasing mortality while on the waiting list. Such trade-offs need to be balanced to optimize patient outcomes.

In addition, the decision regarding the optimal time to treat HCV should take into account limited monetary resources. The high price of DAAs has created concerns about their impact on health care budgets, delaying timely treatment for many HCV patients, and has led to a debate about the value and affordability of these drugs.[6] Three recent studies addressed this topic but reached conflicting conclusions: 2 studies concluded that pre-LT HCV treatment always is cost effective,[7,8] whereas another study concluded that pre-LT HCV treatment is cost effective if patients' MELD score is 25 or less and post-LT treatment is cost effective if their MELD score is higher than 25.[9] Therefore, the objective of our study was to generate evidence for the optimal timing of HCV treatment by determining the cost effectiveness of pre-LT vs post-LT HCV treatment with approved oral DAAs in decompensated cirrhotic patients on the waiting list.

Materials and Methods

Model Overview

We used a validated, individual-level, state-transition model of liver transplant candidates, that simulated a virtual trial comparing long-term outcomes of pre-LT vs post-LT HCV treatment with oral DAAs.[10] The model simulated the lifetime course of patients on the transplant waiting list and after LT (Figure 1). The model's outcomes were validated using data from the United Network for Organ Sharing (UNOS). In this analysis, we extended that model to evaluate the cost effectiveness of pre-LT vs post-LT HCV treatment. We used a weekly cycle to advance time in the model and simulated 1 million patients to reduce simulation noise.

Baseline Population

We simulated patients with decompensated cirrhosis (without hepatocellular carcinoma) infected

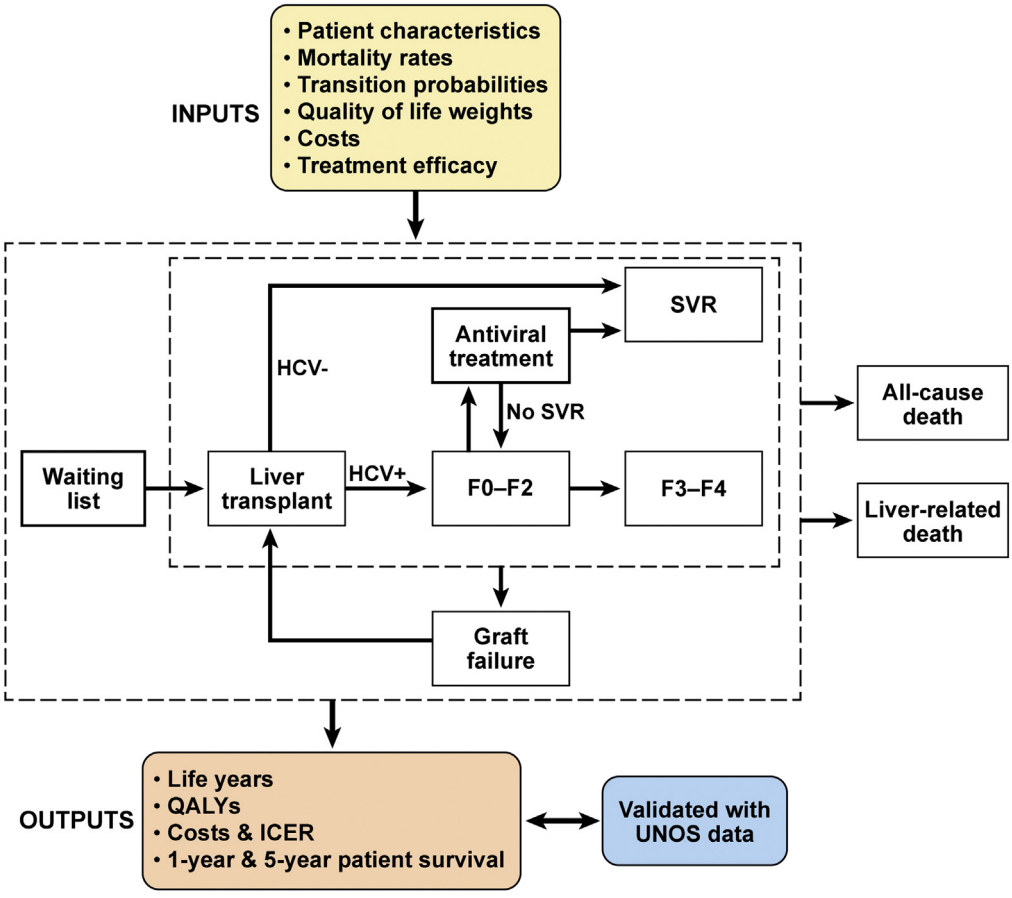

Figure 1. Model schematic showing the flow of patients pre- and post-LT. For each patient profile, the model simulated 2 treatment strategies: (1) pre-LT HCV treatment with DAAs, and (2) post-LT HCV treatment with DAAs. OPTN, Organ Procurement and Transplantation Network.