Economic Comparison of Serologic and Molecular Screening Strategies for Hepatitis C Virus

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Abstract: Background: Hepatitis C virus (HCV) screening is traditionally performed using an enzyme-linked immunosorbent assay (ELISA), and HCV infection is confirmed by measuring the viral load using polymerase chain reaction (PCR). An alternative screening approach is to use only PCR, without the ELISA pretest. **Methods:** We compared the cost ratio of screening for HCV using 2 approaches: (1) ELISA followed by PCR testing, and (2) PCR testing alone. The results were analyzed using a decision analysis model. A sensitivity analysis and a threshold analysis were performed by varying both the prevalence of HCV infection (to encompass populations in which viral infection is overrepresented) as well as the costs of PCR testing. **Results:** Under baseline assumptions, the costs of PCR testing alone were substantially greater than the combination of ELISA and PCR testing. The cost per patient screened using combination testing was $42.30, whereas testing with only PCR cost $200.00 per patient. The prevalence of HCV had a greater impact on the cost ratio than did the costs of laboratory tests. The use of PCR testing alone became less costly only when the prevalence of HCV infection was greater than 69.5%. Otherwise, the costs of the 2 approaches were similar when the cost of PCR was 1% of that of ELISA. **Conclusion:** From a pharmacoeconomic basis, the current approach of HCV screening (ie, using ELISA and PCR testing) was found to be the less expensive screening strategy in a general US population and for most cohorts in which HCV infection was noted to be overrepresented. Screening for HCV is less costly using solely PCR testing only when the prevalence of HCV infection is greater than 69.5%.

Hepatitis C virus (HCV) infection is defined by the presence of viral replication as measured by polymerase chain reaction (PCR). Chronic HCV infection can lead to both hepatic and nonhepatic disorders.[1] The hepatic manifestations include progressive fibrosis, cirrhosis, hepatocellular carcinoma, and hepatic failure, whereas the nonhepatic manifestations can

include cryoglobulinemia, insulin resistance, and renal insufficiency.[2,3] Achieving a cure with antiviral therapy improves clinical outcomes such as quality of life and survival.[4-6] Current treatment revolves around the use of all-oral direct-acting antiviral agents that are safe, tolerable, and highly effective.[7]

The Centers for Disease Control and Prevention estimates that approximately 1% of the US population is infected with HCV.[8] However, certain cohorts of patients, such as those who are undergoing hemodialysis or who are incarcerated, may have higher rates of infection.[9,10] Although the diagnosis of HCV infection is straightforward and relies on a commonly available laboratory blood examination, a number of barriers exist to curing patients infected with HCV, including the cost of therapy, identifying who is infected, and linkage to additional care.[11] Several tests are available for determining the presence of HCV infection,[12,13] the most common being an enzyme-linked immunosorbent assay (ELISA). If antibodies are detected with this modality, HCV infection can then be confirmed by the presence of a viral load as measured by PCR.

Screening for HCV infection is, therefore, a 2-step process. However, the standard approach of detecting HCV antibodies requires a follow-up blood test, which can result in a loss of patients who need extra testing. HCV screening programs have demonstrated that up to 10% of individuals who test positive for HCV antibodies fail to undergo the required additional testing of their viral load.[14-17] Furthermore, the uncertainty of infection following the detection of HCV antibodies may lead to feelings of fear or anxiety.[18] An alternative screening strategy is to test only once by assessing for the presence of viral replication with PCR.

We sought to compare the costs associated with 2 screening strategies used to make a diagnosis of chronic HCV infection in a US setting. One strategy is to screen with ELISA and, if the results are positive, confirm with PCR testing. The other strategy is to screen all patients using PCR without prior ELISA testing. We hypothesized that the costs of both strategies may be similar in cohorts in which HCV is highly prevalent.

Methods

The costs of the 2 approaches were compared using cost ratio; a cost ratio below 1 favored ELISA followed by PCR testing, whereas a cost ratio above 1 favored testing with PCR alone.

Analysis

The costs of ELISA and PCR blood tests vary substantially among laboratories. Even within a particular laboratory, the costs of each blood test can differ. Thus, the costs of ELISA were held constant and the costs of PCR testing were varied by incremental multiples of the costs of ELISA in order to compare the 2 screening approaches. The costs of ELISA were obtained from a sampling of commercial laboratories in the Los Angeles area. A multiple of 5 was used as the baseline. The spectrum of cost differences encompassed the range of cost differences for the laboratories that were queried. The cost for blood draws was included in the cost of the blood tests. All costs were in US dollars.

A HCV prevalence of 0.01 was used as the baseline value. We varied the value to encompass the range described in several HCV-endemic populations.[8,19] A base population of 10,000 patients was utilized in the model. The specificity of the ELISA test was assumed to be 85%.

A threshold analysis was performed to assess the values that identified the least costly strategy. Study variables, including seroprevalence and PCR costs, were varied over time. Societal perspective was taken for the study. Given the short time horizon of the study, discounting was not applied to the model.

Assumptions

Two important assumptions were made in our model. First, we assumed 100% specificity and sensitivity of PCR testing. Second, we assumed complete follow-up of ELISA-positive patients with further PCR testing.

Results

Using our baseline assumptions, we found that the costs associated with the combined ELISA and PCR testing were substantially lower than those of PCR testing alone ($423,000 vs $2,000,000, respectively). The cost per patient was also less expensive with 2-step testing ($42.30) compared with single-step testing ($200.00). The model was dependent on the costs of laboratory tests and the prevalence of HCV infection. As the costs of PCR testing decreased relative to HCV infection prevalence, the cost ratio increased, favoring PCR testing alone. Likewise, the cost ratio favored single-step testing as the HCV infection prevalence increased.

The prevalence of HCV infection was varied in our model in order to encompass the range seen in endemic populations. ELISA plus PCR testing was the preferred screening approach until the prevalence of HCV infection reached 69.5%. At this seroprevalence, the costs were equal between the 2 strategies. Above a seroprevalence of 69.5%, PCR testing alone was less costly.

We also varied the costs of PCR testing as a multiple of ELISA costs. For the costs of the strategies

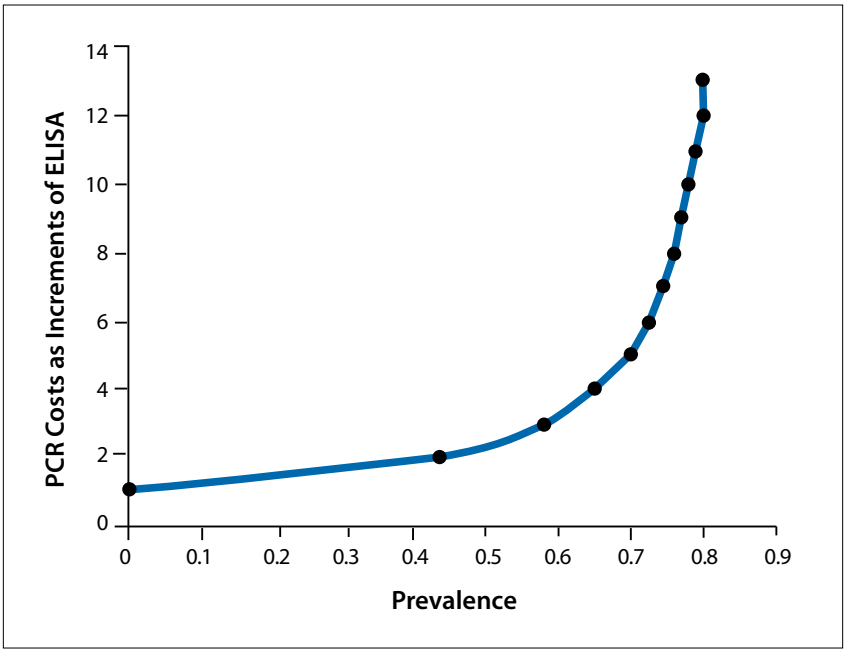

Figure. Two-way sensitivity analysis varying the seroprevalence of hepatitis C virus and costs of polymerase chain reaction (PCR) testing. Values below the threshold line favor PCR-only testing, and values above the threshold line favor combined enzyme-linked immunosorbent assay (ELISA) and PCR testing.

to be similar, the cost of PCR testing must be within 1.01125% of that of ELISA. In a 2-way sensitivity analysis, the costs of both strategies were equal as the prevalence of HCV infection increased and the costs of PCR testing decreased (Figure).

Discussion

Screening involves testing for a disease in individuals without any of the disease's associated signs or symptoms. Identifying patients with HCV infection in particular can lead to harm reduction through counseling regarding alcohol and HCV transmission. Moreover, patients with advanced liver disease can undergo surveillance for hepatocellular carcinoma. All HCV-infected patients should be considered candidates for antiviral therapy. Although tests for HCV infection have been widely available, HCV screening was not originally well accepted in the United States, partly due to the fact that antiviral treatment options were limited by adverse effects.[18] With the availability of safe and effective therapy using direct-acting antiviral agents, screening for HCV infection was accepted, and its target population expanded to include Baby Boomers.[20]

The population recommended for HCV screening has evolved as a reflection of better understanding of the epidemiology of HCV and the availability of direct-acting antiviral agents. Historically, screening for HCV was focused on patients with known risk factors for HCV transmission.[21] Because a large number of patients with HCV infection are Baby Boomers who are unaware of their infection, a 1-time screening program of individuals born between 1945 and 1965 is recommended.[13]

Screening for HCV involves first testing with an ELISA, and then confirming whether an infection exists by measuring the viral load, typically with PCR testing. Other modalities for HCV screening have been studied, such as finger stick and oral swab testing.[22] However, similar to the ELISA, these modalities indicate HCV exposure and not necessarily infection. Sequential testing with ELISA and tests to assess for viral replication may be cumbersome and time-consuming, as it involves follow-up laboratory tests. This combined approach differs from the testing for another hepatotropic virus, hepatitis B virus. With hepatitis B virus, the results of a single blood work are used to simultaneously screen and make a diagnosis of viral infection.[23,24]

Thus, we sought to compare the costs associated with standard screening (ELISA followed by testing with PCR) with the costs associated with assessing the viral load as the initial step. The results of our study indicate that assessing the viral load as the initial step becomes less costly vs using ELISA first only when the overall costs of ELISA and PCR testing are similar or when the prevalence of HCV infection is above 69.5%.

There are a number of important limitations in our study. We assumed 100% follow-up for patients who were found to have HCV antibodies. This is not consistent with prior observations, but is a bias against the model.[25] If the time horizon of the model included the natural history of the viral infection, higher costs would be expected due to a missed diagnosis. The model also

did not account for any determinants of linkage to further testing, such as race or ethnicity, age, insurance type, comorbidities, and site of testing.[14,26-28] These factors are all likely to affect compliance with an ELISA. Another limitation is that we did not consider laboratory reflex testing with the ELISA. For routine screening, reflex testing would obviate the need for a second laboratory visit. Our model also did not capture scenarios in which single-step testing is preferred. Although the use of single-step testing with PCR was found to be too costly for routine screening in our model, there are situations in which it may be considered medically necessary to screen using PCR. For example, HCV antibodies may not be immediately detectable in patients with acute infection.[29,30] In these circumstances, patients suspected of having acute HCV infection should be tested using PCR.

Conclusion

The results of this study indicate that the less costly HCV screening strategy is the commonly practiced approach of screening with ELISA first, followed by PCR testing. Even in highly prevalent cohorts, ELISA-based screening is preferred economically. Screening with PCR is economically feasible only when the prevalence of HCV infection is greater than 69.5%.

The authors have no relevant conflicts of interest to disclose.

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