



# How to Optimize the Care Cascade of Hepatitis C Virus Infection

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See “The Korean Hepatitis C Virus Care Cascade in a Tertiary Institution: Current Status and Changes in Testing, Link to Care, and Treatment” by Jonggi Choi, et al. on page 964, Vol. 16, No. 6, 2022

Chronic hepatitis C virus (HCV) infection is currently a major cause of liver disease, affecting approximately 71.1 million people worldwide.<sup>1</sup> It ultimately results in development of liver cirrhosis and/or hepatocellular carcinoma (HCC), if left untreated. The prevention of disease transmission through an effective vaccination against HCV might be ideal, however, it still remains elusive. So, early detection of HCV infection and appropriate treatment are the best way in the real-life practice to reduce the overall disease burden from chronic HCV infection. Since HCV screening was introduced among blood donors in 1992, the overall cases of HCV transmission have been remarkably decreased.<sup>2</sup> However, chronic HCV infection still remains the second-most common cause of chronic liver diseases in the Republic of Korea. Primarily owing to the availability of highly efficacious oral direct antiviral agents (DAAs) with less adverse events in the mid-2010s,<sup>3</sup> the elimination of HCV infection promoted by the World Health Organization will have become achievable in the near future.<sup>4</sup> Hence, in order to accomplish such a goal, the current practice guideline generally recommends early detection and treatment of patients with chronic HCV infection to prevent progression to liver cirrhosis and/or HCC as well as newly infected case.<sup>5,6</sup> Nowadays, considering the high sensitivity and specificity of anti-HCV test for screening, the global attitudes have favored universal HCV screening among the general population. Indeed, the Centers for Disease Control and Prevention recommends HCV screening at least once per lifetime in all adults, except in locations where the prevalence of HCV infection is <0.1%.<sup>7</sup> However, such universal screening programs have not yet

been included in the Korean National Health Program due to the low prevalence in the Republic of Korea. So, it is regarded as the first and representative obstacle against the appropriate HCV care cascade.

In this issue of *Gut and liver*, Choi *et al.*<sup>8</sup> comprehensively assessed the changes in the HCV care cascade and current status, i.e., HCV test, linkage to care, and treatment and long-term prognosis, in the Republic of Korea, based upon 1,144,468 patients who received anti-HCV test for the past two decades in a single tertiary referral hospital. About 30% of the study population with anti-HCV positivity did not receive the subsequent HCV RNA test. Among patients receiving HCV RNA test, about two-thirds had HCV RNA positivity. Patients who did not have HCV RNA tests were older and more likely to have a non-HCC malignancy, normal alanine aminotransferase level, and good liver function. Based upon these findings, we can cautiously speculate that physicians might have misconceptions that a normal alanine aminotransferase or absence of overt HCC reflects a lack of liver damage, thereby not requiring further tests. In addition, when diagnosed as anti-HCV positivity in the surgery departments and health check-up, patients were relatively unlikely to be referred to hepatologists, which is a well-known barrier in the appropriate control of chronic HCV infection. Nevertheless, it is encouraging that the linkage time from anti-HCV positivity to HCV RNA test has dramatically improved. This phenomenon might be in part because the general caring system and increase in HCV infection awareness among physicians have gradually improved, even though the level of awareness is still unsatisfactory. However, we should recognize that the



rate of successful linkage from anti-HCV positivity to HCV RNA test might be much lower in the real-world primary care setting, considering that the reported rate of “70%” in this study derived from the largest tertiary referral hospital in the Republic of Korea. Therefore, further population-based study at the nationwide level might be required to elucidate this issue.

Notably, among patients with chronic HCV infection, those who were not treated were older, and more of them had higher levels of alanine aminotransferase, cirrhosis, and a history of HCC and non-HCC malignancy than those receiving antiviral treatment with statistical significance. It is most likely because physicians and/or patients might have significant concern about both the adverse effects during the treatment using the regimen of pegylated interferon plus ribavirin for 24 to 48 weeks and the relatively lower rate of sustained virological response in the pre-DAA era. In the similar context, the average yearly rate of antiviral change, ranging from 28.3% in 2011 to 38.8% in 2016 and the number of patients treated with an interferon-containing regimen has remarkably decreased since 2015. Furthermore, linkage times for HCV RNA test from anti-HCV positivity and for uptake of antiviral treatment from HCV diagnosis decreased notably after 2015, when highly efficacious oral DAAs became available in the Republic of Korea.

Successful HCV elimination requires the establishment and maintenance of all steps in the care cascade,<sup>9</sup> starting with the appropriate management of decreased awareness among physicians and/or patients. Among them, universal screening programs to detect asymptomatic patients with chronic HCV infection might be likely the most important step to reduce the overall HCV-related disease burden. For example, one-time universal HCV screening program among the population aged 40 to 65 years in the Republic of Korea also seems cost-effective from both the healthcare system and societal perspectives.<sup>10</sup> However, the optimal timing and frequency of HCV screening remain to be determined yet. In addition, beyond the early detection and treatment of HCV-infected case through universal HCV screening program, the more delicate approach, e.g., HCV reflex test followed by automatic appointments and a late call-back strategy, might facilitate HCV care cascade.<sup>9</sup> Further studies are required to optimize these plans from the viewpoints of the epidemiology and health policy.

In conclusion, elimination of HCV will require a strong commitment from governments and payors to support financial resources covering from education for physicians and/or patients, diagnosis, to treatment. Furthermore, along with universal HCV screening, to define targeted populations and monitor risk behaviors according to the

individualized hazards will have an additional role in achieving the goal of eliminating HCV.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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