Serologic vs. molecular testing for screening for hepatitis C virus infection in patients with hematologic malignancies with and without prior hematopoietic cell transplant.

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Poster # 911016

Abstract

- The optimal screening test for hepatitis C virus (HCV) in cancer patients has not been established.
- Testing for antibody to HCV (anti-HCV) is a low-cost diagnostic method in widespread use worldwide.
- We sought to identify the most appropriate screening test for HCV in patients with hematologic malignancies and/or prior hematopoietic cell transplant.
- Patients who were seen at the Lymphoma/Myeloma, Leukemia, and Stem Cell Transplant clinics from February through November 2019, were simultaneously screened for HCV with serologic (anti-HCV) and molecular (HCV RNA) assays.
- A total of 214 patients were enrolled in the study, of whom 127 (59%) were men and 180 (84%) were white. One hundred forty-nine patients (70%) had a lymphoid neoplasm, and 15 (7%) underwent HCT. Three patients (1.4%) had positive anti-HCV, and two (0.9%) had positive HCV RNA. The overall percentage agreement was 99.5% (95% CI, 97.4% to 99.9%). There were no cases of seronegative HCV infection.
- The diagnostic yield for screening for chronic HCV infection in immunocompromised cancer patients is similar for serologic and molecular testing. The use of anti-HCV, a diagnostic method with low cost, in patients with cancer would contribute to HCV elimination.

Introduction

- Chronic HCV infection causes significant morbidity and mortality in patients with cancer and can interfere with cancer treatment.
- Estimates of the prevalence of chronic HCV infection among cancer patients in the US range from 1.5% to 10.6%.
- Two types of assays are approved for the diagnosis of HCV infection: Serologic assays that detect antibody to HCV (anti-HCV) and Molecular assays (HCV RNA)
- Serologic assays cost less than molecular assays US$ 0.50-1.70 vs. US$ 30-200.
- U.S. national guidelines recommend screening with anti-HCV in both immunocompetent and immunocompromised patients, but anti-HCV-based screening may be unreliable in some immunocompromised patients (HCT recipients).
- We sought to identify the most appropriate screening test for HCV in patients with hematologic malignancies and/or prior hematopoietic cell transplant.

Methods

- Cancer patients who were seen at the Lymphoma/Myeloma, Leukemia, and Stem Cell Transplant clinics at MDACC (Feb 2019 - Nov 2019) were enrolled prospectively.
- Patients ≥ 18 y/o with any type of hematologic malignancy with or without HCT never screened for HCV. Anti-HCV and HCV RNA tests were performed simultaneously.
- Anti-HCV testing was performed by using the ARCHITECT Anti-HCV assay (Abbott Laboratories), specificity of 99.60% (95% CI, 99.45% to 99.71%), sensitivity of 99.10% (95% CI, 96.77% to 99.89%).
- HCV RNA testing was performed by using the Cobas HCV test (Roche Molecular Systems, Inc.). The quantification range 15 IU/mL to 100,000,000 IU/mL (1.18 log IU/mL to 8.00 log IU/mL).
- Using McNemar's test, 214 patients were needed to be enrolled to yield 90% power to detect a significant difference ($p<0.05$) in diagnostic performance between the two tests.
- The agreement between the two tests was evaluated using Cohen's kappa statistic and McNemar's test.
- All tests were two-sided with a significance level of 0.05. Data analyses were performed using SAS version 9.3 (SAS Institute Inc.).
- **Funding:** Investigator-initiated study sponsored by Merck & Co., Inc. also supported in part by the National Cancer Institute (P30CA016672).

Results

- A total of 214 patients were enrolled in the study. Of these, 127 (59%) were men, and 180 (84%) were white. One hundred forty-nine patients (70%) had a lymphoid neoplasm, 65 (30%) had a myeloid neoplasm, and 15 (7%) underwent HCT. One hundred one patients (47%) had stable disease, and 93 (43%) had progressive disease.
- Three patients (1·4%) had positive anti-HCV test results, and two (0·9%) had positive HCV RNA test results (Table 1).
- The overall percentage agreement was 99·5% (95% CI, 97·4% to 99·9%). Of the three patients with positive anti-HCV test results, 2 had positive and 1 had negative HCV RNA test results. There were no cases of seronegative HCV infection, i.e., of the 214 patients with negative anti-HCV test results, all had negative HCV RNA test results too. (Figure 1)
- The positive percentage agreement was 66·7% (95 CI, 20·8% to 93·9%), and the negative percentage agreement was 100·0% (95% CI, 98·2% to 100·0%). Cohen's Kappa coefficient was 0·80 (95% CI, 0·41 to 1·00, p <0·0001), indicating substantial agreement between anti-HCV and HCV RNA tests for diagnosis of HCV infection. Consistent with this, McNemar's test showed no significant difference in the overall performance between these two tests (p=0·32).
- One patient with a negative anti-HCV test result had an inconclusive HCV RNA test result, but a repeated HCV RNA test produced a negative result.

Figure 1. Serologic vs molecular testing for HCV screening in cancer patients.

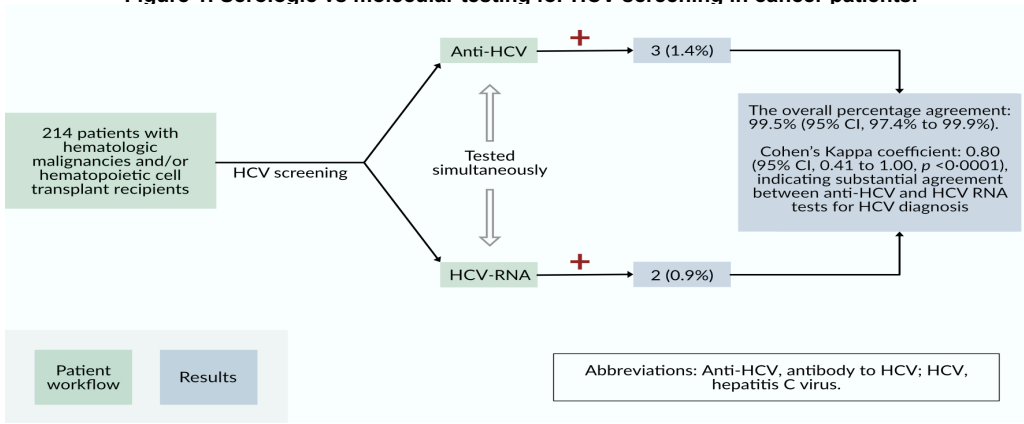

Table 1: Characteristics of the study population (n=214)

Characteristic	Value
Median age, (range, years)	64 (27-84)
Male sex	127 (59%)
White	180 (84%)
Lymphoid neoplasm*	149 (70%)
Myeloid neoplasm†	65 (30%)
HCT	15 (7%)
Allogeneic	3/15 (20%)
Autologous	12/15 (80%)
Anti-HCV positive	3 (1%)
HCV RNA positive	2/3 (67%)
HCV RNA negative	1/3 (33%)
HCV RNA positive	2 (1%)
Anti-HCV positive	2/2 (100%)
Anti-HCV negative	0/2
1b	2/2 (100%)

HCT=hematopoietic cell transplant; HCV=hepatitis C virus.
*Lymphoid neoplasms included the following categories based on the 2016 World Health Organization classification: mature B-cell neoplasms and Hodgkin lymphoma.
†Myeloid neoplasms included the following categories based on the 2016 World Health Organization classification: myeloproliferative neoplasms, myelodysplastic/myeloproliferative neoplasms, myelodysplastic syndromes, acute myeloid leukemia and related neoplasms, and B-lymphoblastic leukemia/lymphoma.

Conclusion

- The diagnostic yield for screening for chronic HCV infection in heavily immunocompromised cancer patients is similar for serologic and molecular testing.
- The use of diagnostic methods with low cost such as anti-HCV would contribute to the long-term goal of eliminating HCV infection in the U.S. and globally.