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Implementation of Universal Hepatitis C Virus Screening in a Tertiary Cancer Center

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Abstract

Background: The prevalence of chronic hepatitis C virus (HCV) infection in the United States is ≤1%. Universal HCV screening is recommended nationwide. Here we describe our experience implementing universal HCV screening at a cancer center.

Methods: In October 2016, universal HCV screening with HCV antibody (anti-HCV) was initiated for all new outpatients. Universal screening was promoted through widespread provider education, orders in the Epic electronic health records (EHR), SmartSets, and automated EHR

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Authors' contributions

Dr. Torres is the guarantor of the article. Dr. Torres designed the study, provided study patients, analyzed and interpreted the data, and co-wrote the manuscript. Dr. Mustafayev performed research, analyzed and interpreted the data, performed statistical analysis, designed tables and figures, and co-wrote the manuscript. Ruston P. Juneau analyzed and interpreted the data. All authors were involved in the drafting, review, and approval of the report and the decision to submit it for publication.

Declaration of interests

Dr. Torres is or has been the principal investigator for research grants from the National Cancer Institute, Gilead Sciences, and Merck & Co., Inc., with all funds paid to MD Anderson Cancer Center. Dr. Torres is or has been a paid scientific advisor for Dynavax Technologies, AbbVie, Inc., Gilead Sciences, Janssen Pharmaceuticals, Inc., and Merck & Co., Inc.; MD Anderson Cancer Center is managing the terms of these arrangements in accordance with its conflict-of-interest policies. The other authors report no conflicts of interest.

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reminders. The effort focused on patients with solid tumors as universal screening in patients with hematologic malignancies was already standard practice. The primary outcomes were the proportion of patients screened and the proportion of patients with reactive anti-HCV test results linked to HCV care. The secondary outcome was the incidence of HCV-associated hepatocellular carcinoma as a second primary malignancy (HCC-SPM) in patients with history of other cancers before HCC diagnosis. Epic's Reporting Workbench Business Intelligence tools were used. Statistical significance was defined as $p<0.05$ on chi-square analysis.

Results: Between April 2016 and April 2023, 56,075 patients with solid tumors were screened for HCV, of whom 1,300 (2.3%) had reactive anti-HCV test results. The proportion of patients screened was 10.1% in the 6 months before study implementation and 34.4% in the last 6 months of the study ($p<0.001$). HCV screening was ordered using SmartSets in 39,332 patients (45.8%) and in response to automated EHR reminders in 10,972 patients (12.8%). Most patients with reactive anti-HCV test results were linked to care (765/1300; 59%), most with proven HCV infection were treated (425/562; 76%), and most treated patients achieved sustained virologic response (414/425; 97%). The incidence of HCC-SPMs was 15% in historical controls treated during 2011–2017 and 5.7% following implementation of universal screening ($p=0.0002$).

Conclusions: Universal HCV screening can be successfully implemented in cancer hospitals using an EHR-based multipronged approach to eliminate HCV and prevent HCV-associated HCC-SPMs.

Keywords

Cancer; hepatitis C virus; screening; best practice alerts; linkage to care; elimination

Introduction

Globally, 58 million people are chronically infected with hepatitis C virus (HCV), including an estimated 2.4 million people in the United States (US) alone (1–3). However, approximately 80% of the people infected with HCV worldwide (3) and 40% of the people infected with HCV in the US are unaware of their infection (4). In 2016, the World Health Organization adopted the first global hepatitis plan, which called for the elimination of viral hepatitis as a public health threat by 2030 and established targets for countries to meet to achieve that goal (5). Seventy-six countries, including the US, are not on track to meet the HCV elimination targets by 2050 (3). To achieve global HCV elimination targets, multiple interventions must be implemented to increase population engagement along the HCV care cascade (6). Therefore, the US federal government has proposed a National Hepatitis C Elimination Program to eliminate HCV infection nationwide (7, 8).

In the general US population, the prevalence of chronic HCV infection is ≤1% (2). According to data from the US Centers for Disease Control and Prevention, the rate of reported cases of acute HCV infection in the general US population increased by 400% between 2010 and 2020, likely related to the opioid epidemic (9). Because of the natural history of HCV infection, the majority of cases of acute HCV infection will progress to chronic infection if untreated (10).

The reported prevalence of chronic HCV infection among cancer patients in US cancer centers ranges from 1.5% to 2.4%, but these prevalences may be inaccurate due to the lack of routine HCV screening in many cancer centers (11–13). Chronic HCV infection causes virologic, hepatic, and oncologic concerns in patients with cancer (10). Our group has demonstrated the development of HCV-associated hepatocellular carcinoma (HCC) as a second primary malignancy (HCC-SPM) in patients who presented for treatment of a different primary cancer (14, 15).

Government agencies and cancer professional societies recommend universal HCV screening for cancer patients (4, 8, 10, 16). Here, we describe our experience in implementing universal screening at MD Anderson Cancer Center (MDACC), one of the largest cancer centers in the US and the world and which houses the first clinic in the US devoted to the management of HCV in patients with cancer (17, 18).

Methods

Study Design and Patient Population

In October 2016, universal HCV screening with HCV antibody (anti-HCV) was initiated at MDACC for all new outpatients. Universal screening was promoted through widespread provider education, newly created orders in the electronic health record (EHR) (SmartSets), and automated EHR reminders (Best Practice Alerts or BPAs) in the Epic EHR software. The effort focused on patients with solid tumors as universal screening in patients with hematologic malignancies had been standard since 2006.

The ongoing HCV screening initiative was launched in phases. Starting in October 2016, a SmartSet for HCV screening was made available in the EHR at the initial visit. Beginning in December 2019, for all new patients 18 years of age or older with solid tumors, a reminder or best practice alert was displayed on the EHR screen if the patient had never been tested for HCV including those not screened using new patient SmartSet. This best practice alert was linked to an order for anti-HCV testing. HCV prevalence and linkage to care were assessed after the implementation of SmartSets and best practice alerts. The study was approved by the MDACC Institutional Review Board.

Clinical and Laboratory Parameters

The PRISM HCV assay (Abbott; Abbott Park, IL) was used for all anti-HCV testing. As part of the standard of care, patients with reactive anti-HCV test results were referred to HCV specialists (i.e., specialists in infectious diseases or gastroenterology/hepatology) for additional workup and management. At our center, reflex HCV RNA testing is not required before discussion of anti-HCV results with patients. Multidisciplinary care starts at the patient’s first clinic visit in either the Department of Infectious Diseases or the Department of Gastroenterology/Hepatology. During discussions between patients and HCV specialists, patients were asked about their history of HCV and its treatment, the presence of advanced liver disease, and the history of screening for other carcinogenic viruses (e.g., hepatitis B virus, HIV).

Outcome Assessments

The primary outcomes of the study were the proportion of patients with solid tumors who were tested for HCV after implementation of universal screening and the proportion of patients with reactive anti-HCV test results linked to HCV care. The secondary outcome was the incidence of HCC-SPM after implementation of universal screening; we compared this incidence with the incidence in historical controls from our institution with HCV-related HCC-SPM (14). Epic's Reporting Workbench tools were used to identify the HCV orders. To evaluate the impact of our intervention, we compared the total number of patients tested for anti-HCV in the 6 months before implementation of universal HCV screening (April 2016 to October 2016) and during a 6-month period after implementation of universal HCV screening (October 2022 to April 2023). The outcome was also compared by individual specialty clinics to identify those with lower screening rates.

Definitions

Linkage to care was defined as any attendance to a scheduled appointment in the Infectious Disease or Gastroenterology/Hepatology departments. Proven HCV was defined as reactive anti-HCV test results and detectable HCV RNA. Sustained virologic response was defined as undetectable HCV RNA level at 12 weeks after completion of antiviral treatment. HCC-SPM was defined as development of HCV-associated HCC in a patient with a history of any other type of cancer (14).

Statistical Analysis

Patient characteristics were analyzed using descriptive statistics. All descriptive statistical analyses were carried out using STATA IC software, version 12.0 (StataCorp LP, College Station, TX). Descriptive p-values at a 2-sided significance level of 0.05 were reported. Statistical significance was defined as $p<0.05$ on chi-square analysis.

Results

Of the 85,836 cancer patients screened for HCV during the study period, 56,075 (65.3%) had solid tumors and were further analyzed (Figure 1). HCV screening was ordered using SmartSets in 39,332 patients (45.8%) and in response to best practice alerts in 10,972 patients (12.8%). The proportion of new patients screened increased from 10.1% during the 6 months before study implementation to 34.4% during the last 6 months of the study period ($p<0.001$). The number of patients screened for HCV each month increased over time except during the peak of the COVID-19 pandemic (Figure 3).

The prevalence of reactive anti-HCV test results was 2.3% (1,300/56,075 patients). The highest HCV prevalence rates were seen in patients with gastrointestinal (5.6%), head and neck (4%), and thoracic cancers (4%) (Table 1).

Most of the patients with reactive anti-HCV test results were linked to HCV care (765/1300; 59%), most patients linked to HCV care had proven HCV infection (562/765; 73%), most patients with proven HCV infection were treated (425/562; 76%), and most treated patients achieved a sustained virologic response (414/425; 97%) (Figure 2). Of the 535 patients who

were not linked to care, 370 (69%) were lost to follow-up (many of them seen only for a second opinion from oncologists), 72 (13%) were found not to have chronic HCV infection, likely due to prior exposure and spontaneous clearance, and 93 (17%) died. Of the 425 patients treated, 322 (76%) received treatment before they arrived at the cancer center, and 103 patients (24%) were treated at the cancer center. Of the 137 patients who were not treated, 103 (75%) were not offered direct-acting antiviral treatment because of progressive cancer, 28 (20%) were lost to follow-up, and 6 (4%) were not offered treatment to avoid potential drug-drug interactions (Figure 1).

We identified 402 patients with HCV-associated HCC during the study period. The incidence of HCC-SPM decreased from 15% in the historical control group of patients seen at our institution between 2011 and 2017 (14) to 5.7% (23/402) between 2017 and 2023, following the initiation of universal screening (p=0.0002).

Discussion

To our knowledge, this is the first study focused on universal HCV screening in a large cancer center. We showed the successful implementation of the first institution-wide intervention aimed at HCV testing for all new patients with solid tumors. We found that the universal screening program offers several benefits, including screening of a large number of cancer patients, successful treatment of most identified HCV-infected patients, and significant reduction in the rate of HCV-associated HCC-SPM. Our experience suggests that this EHR-based screening strategy can be implemented by other cancer centers in the US and worldwide.

Of note, the prevalence of anti-HCV positivity among cancer patients in our study was 2.3%, which is higher than the HCV prevalence in the US general population of ≤1% (2). Our findings emphasize the need for increased efforts to identify cases of HCV infection among patients with solid tumors and effective linkage to care, consistent with the goals of the National Hepatitis C Elimination Program (3, 7, 8).

Our study showed an effective way to screen patient using the combination of SmartSets supplemented by best practice alerts carefully designed to capture patients not screened at the initial visit to generate one-time screening without unnecessary repeat testing.

A multicenter prospective study including 3,051 newly diagnosed cancer patients in the US showed that a substantial proportion (31%) of chronically infected patients were unaware of their HCV infection (12), which supports the use of universal HCV screening among patients with cancer. HCV-infected patients can be linked to HCV care, with access to curable direct-acting antiviral treatment to reduce the risk of liver disease progression, allow patients access to cancer clinical trials, prevent HCV-associated primary and second primary cancers, and cure selected HCV-related cancers (11, 13–15, 19).

We found that patients with gastrointestinal, head and neck, and thoracic cancers had the highest prevalence of HCV infection. Previous reports show that head and neck cancers and lung cancer are non-HCC solid tumors with a significantly increased incidence among patients with HCV infection in the US (20).

In our study, nearly two-thirds (59%) of patients with reactive anti-HCV test results were linked to HCV care after implementation of universal HCV screening, 76% of patients with proven HCV infection were treated, and 97% of treated patients achieved a sustained virologic response. These rates were significantly higher than those in previous reports of linkage-to-care programs (21–23). Our study's high linkage-to-care and treatment rates are a significant achievement and are among our most important findings, especially considering that the Polaris Observatory Dashboard reports that only 20% to 30% of detected cases of HCV infection are treated in countries with high-quality patient registries (3). The latest report from the US Centers for Disease Control and Prevention highlights that between 2013 and 2022, only 1 in 6 individuals under the age of 40 years without insurance achieved a virologic cure in the US (24). If HCV is left untreated, these infected patients can develop primary or second primary cancers related to HCV, such as HCC and B-cell non-Hodgkin lymphoma, and also develop extrahepatic manifestations of HCV infection (13).

Our study is the first to address the impact of universal screening on HCV-associated HCC-SPM. We found that the incidence of HCC-SPM significantly decreased after initiating universal screening compared to historical controls from our center (10, 24), which suggests that universal HCV screening, linkage to care and treatment of infected patients is an effective cancer prevention strategy that can save many lives.

The current study has limitations. First, our study was conducted at a single tertiary care cancer center with a particular EHR, and our results may not apply to other centers. Second, 41% of patients were not linked to care, and 24% were not treated. However, the high sustained virologic response rates in this study improved oncologic outcomes as reflected in the reduced rate of HCV-associated HCC-SPMs. Third, despite the significant increase in HCV screening rates due to universal screening during the study period, the COVID-19 pandemic led to a decrease in new HCV infection diagnoses, as reported in many countries (3). Fourth, we did not perform a cost-effectiveness analysis, but previous studies have shown that HCV screening and treatment are cost-effective (25, 26). Fifth, the HCV screening is still not reaching all new cancer patients. It is possible that the use of other available support tools (e.g. Health Maintenance) or EHR softwares might improve screening rates. Needless to say, successful screening and microelimination programs require a multidisciplinary team including screening champions, HCV specialists, pharmacists, case managers, patient navigators, EHR team members, and hospital leadership.

Conclusions

The prevalence of HCV infection remains higher in cancer patients than in the general population. Our experience shows that universal HCV screening can be successfully implemented in cancer hospitals nationwide using an EHR-based multipronged approach. The high rates of screening, linkage to care, and HCV treatment in our study may positively affect HCV elimination targets and prevent HCV-associated HCCs, leading to improved public health outcomes.

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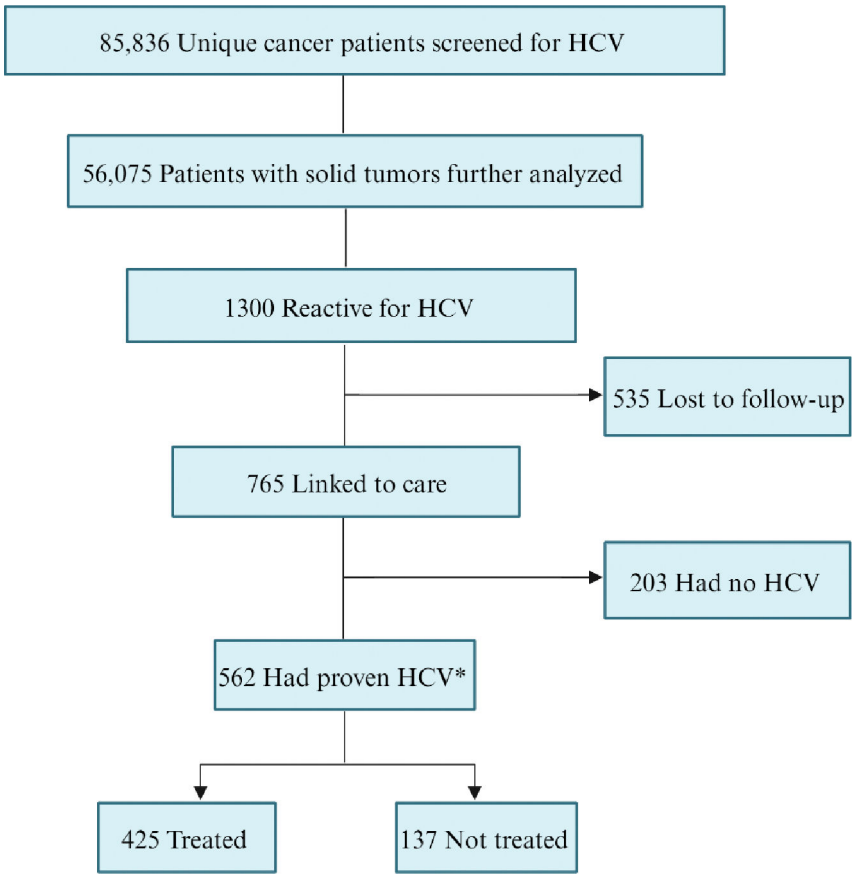

Figure 1.

Flow diagram of study participants. HCV, hepatitis C virus.

*Of the 562 patients with proven HCV, 236 (42%) had cirrhosis with most of them (174 or 74%) having compensated cirrhosis.

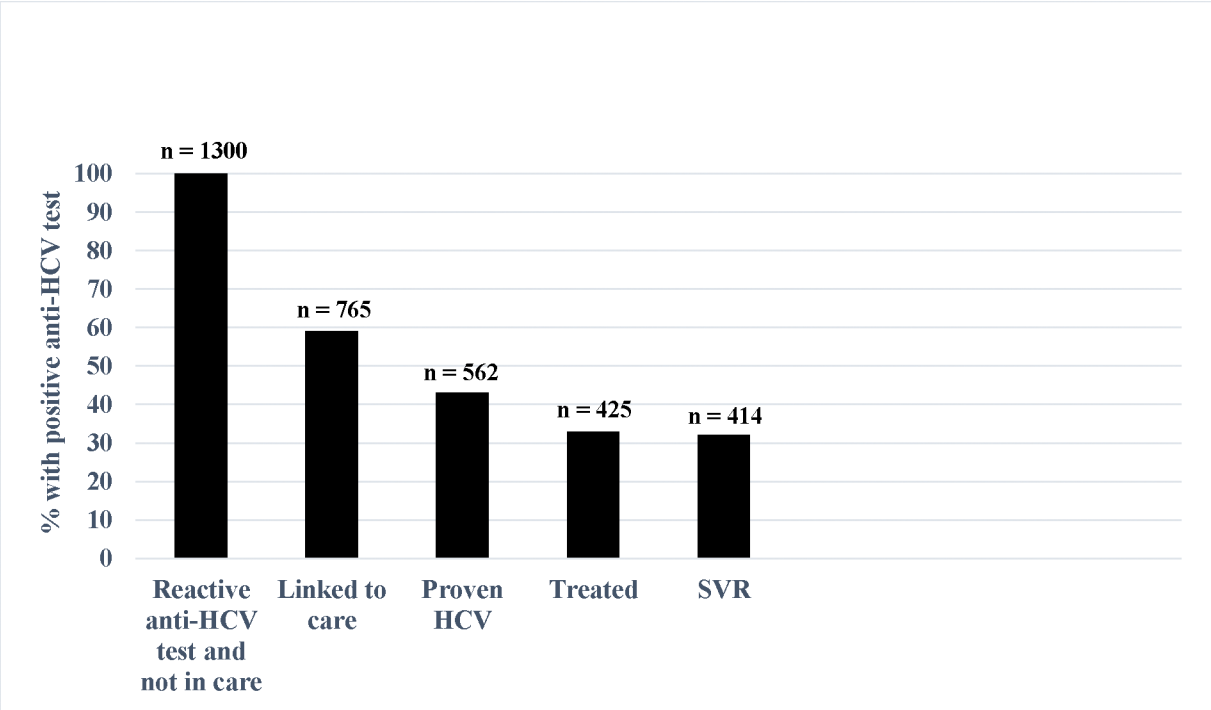

Figure 2.

The cascade of care for patients with solid tumors and positive anti-HCV test results after implementation of universal HCV screening. HCV, hepatitis C virus; SVR, sustained virologic response.

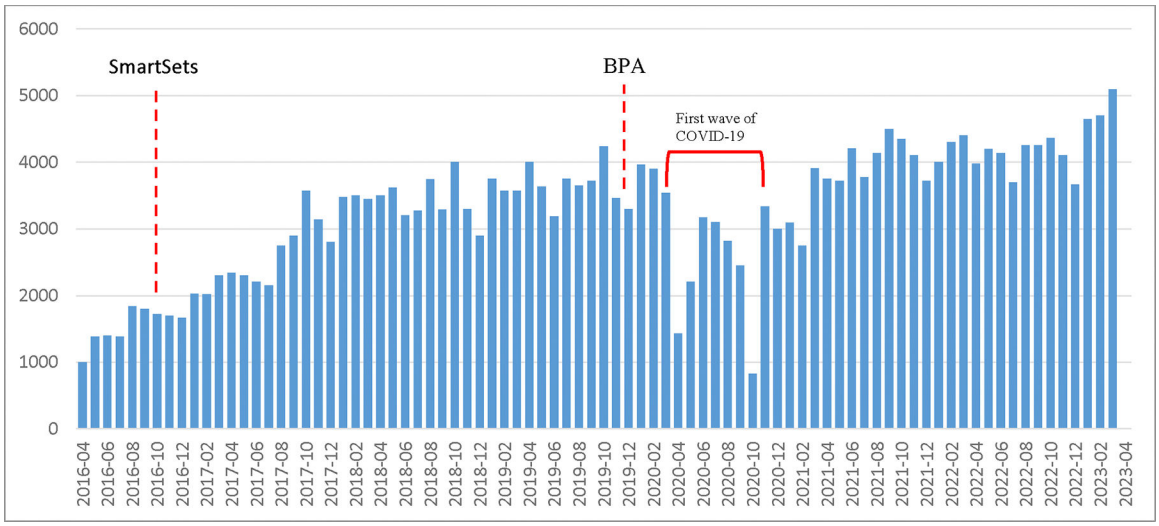

Figure 3.

Number of orders for hepatitis C virus screening by month, April 2016 through April 2023. BPA, best practice allert; COVID-19, coronavirus disease 2019.

The chart shows that the implementation of HCV screening for linking solid tumor patients to care increased the total number of screened patients (linear increase).

Table 1.

Numbers of new patients with solid tumors tested for anti-HCV after implementation of universal HCV screening and test results, by clinic

Clinic	No. of patients tested	Reactive test results, n (%)	Nonreactive test results. n (%)
Brain and Spine Oncology	941	10 (1.06)	931 (99)
Breast Medical Oncology	2970	49 (1.6)	2921 (98.3)
Clinical Center for Targeted Therapies	293	7 (2.98)	286 (97.02)
Endocrine Oncology	7135	57 (0.8)	7078 (99.2)
Gastrointestinal Medical Oncology	8623	483 (5.6)	8140 (94.4)
Genitourinary Medical Oncology	6234	139 (2.2)	6095 (97.8)
Gynecologic Oncology	6026	73 (1.2)	5953 (98.8)
Head and Neck Medical Oncology	2317	92 (4)	2225 (96)
Melanoma Medical Oncology	2190	33 (1.5)	2157 (98.5)
Sarcoma Medical Oncology	1702	22 (1.3)	1680 (98.7)
Thoracic Medical Oncology	3148	125 (4)	3023 (96)
Others	14,496	210 (1.4)	14,286 (98.6)
All	**56,075**	**1300 (2.6)**	**54,775 (97.3)**

Abbreviations; HCV, hepatitis C virus