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Original article

Implementation of an alert system for the care cascade of Hepatitis C infection in patients undergoing elective surgery

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ABSTRACT

Background: A key barrier to an effective care cascade for Hepatitis C virus (HCV) is limited awareness, especially among patients undergoing elective surgery. To address this issue, we introduced an electronic medical record (EMR)-based automatic alert system in 2021 to enhance surgical healthcare providers' awareness of HCV screening and referral rates.
Methods: The alert system was designed to alert surgeons to order preoperative HCV antibody testing for patients undergoing elective surgery before admission and, at discharge, recommend hepatology consultation for patients with positive HCV antibody testing.
Results: The system significantly improved the HCV screening rate by 73,834 (96.8 %) among 76,310 patients undergoing surgery after system implementation, compared to 106,854 (82.8 %) among 129,065 patients between 2016 and 2020 ($P < 0.001$). Among them, the system alerted 12,048 (16.3 %) cases, and 463 patients tested positive for HCV antibodies. However, only 42 (15.3 %) were referred out of 275 (59.4 %) who required hepatology consultation. Linkage failure was associated with other surgery departments than hepatobiliary and transplant surgery departments (odds ratio [OR]=5.940, 95 % confidence interval [CI], 3.080–12.410, $P < 0.001$) and shorter hospitalization duration (OR=0.980, 95 % CI, 0.950–0.990, P = 0.012).
Conclusion: The EMR-based automatic alert system effectively increased HCV screening for patients undergoing elective surgery before admission. However, it could not link them to care cascade in surgery departments. Combining more proactive approaches would be beneficial, such as reflex testing or a call-back strategy.

Introduction

Hepatitis C virus (HCV) infection often progresses silently to cirrhosis and hepatocellular carcinoma [1,2]. The recently reported annual incidence of HCV infection in South Korea was 11.9 cases per 100,000 population, higher than the World Health Organization's impact target of five [3]. The linkage-to-care rate and the treatment rate in South Korea were limited to 65.5 % and 56.8 %, respectively, below the global targets of 90 % and 80 % [3]. HCV infection can be effectively cured with direct-acting antiviral (DAA) treatment, making early diagnosis and eradication essential [4–7]. However, barriers hinder the care cascade, including initial screening for HCV antibody positivity, HCV RNA testing, diagnosis with HCV RNA confirmation, and the subsequent linkage to follow-up care [8,9]. A disparity between medical and surgical departments in awareness about HCV infection has been reported [8]. Literature has also reported insufficient HCV RNA confirmation rates ranging 13.1–44.6 %, suggesting that a lack of awareness on HCV infection is a key barrier in HCV care cascade [8,10,11].

HCV is frequently transmitted via blood-borne route [12], prompting the Korean National Health Insurance System (KNHIS) provides reimbursement for preoperative HCV antibody testing since 2016, thereby minimizing the risk of HCV infection to healthcare workers. In addition, patients undergoing preoperative HCV antibody tests have an opportunity for early management of silent

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HCV infection through proper hepatology consultation during admission for surgery.

To address this, we developed an automatic alert system implemented to the electronic medical record (EMR) system in 2021, and assessed the effectiveness of the EMR-based automatic alert system (referred to as the Alert system) in identifying potential HCV infections and streamlining the referral process for comprehensive care in a Korean tertiary medical hospital.

Material and methods

Implementation of the alert system for patients undergoing surgery

We developed and implemented the Alert system in January 2021 at Yonsei University Severance Hospital for patients scheduled to undergo surgery under general endotracheal anesthesia (GEA). The Alert system comprised two steps. The ***"first step"*** involved automatic screening for HCV antibody test results within 3 years at the time of prescribing admission order, including preoperative assessments (Supplementary information 1), for undergoing elective surgery. If no test result was available, an alert was triggered to automatically prescribe the HCV antibody test. Consequently, the system could generate an alert even in cases where for the recently prescribed HCV antibody tests that had not been conducted yet. The ***"second step"*** involved automatic alert to the surgeon prescribing discharge, prompting them to initiate a hepatology consultation and refer patients with a positive result for the HCV antibody test at the time of discharge after the completion of postoperative management (Fig. 1).

The automatic generation of additional tests (e.g., HCV antibody or HCV RNA test) or referral processes without the patient's consent could violate the Personal Information Protection Act in South Korea. Therefore, the Alert system does not directly issue prescriptions, but alerts the surgeon to instruct the testing and referral process to the hepatology department by obtaining patient's consent.

Study design

We conducted a retrospective study to determine whether any changes occurred in the care cascade of HCV after implementing the Alert system. First, for the *Test group*, we retrospectively reviewed the patients who had been listed by the Alert system between January 2021 and June 2023. Second, for the *Control group* (before implementing of the Alert system), we reviewed the patients who underwent elective surgery under GEA between January 2016 and December 2020, considering the reimbursement of HCV antibody test by the KNHIS since 2016. Cases were excluded that were (1) emergent, (2) simple procedures (e.g., open dressing, open biopsy procedures, intraoperative ablation therapy, tracheostomy in the intensive care unit, and endoscopic procedures), (3) duplicated in the same patients, and (4) performed in < 19-year-old. Testing methods for HCV antibody and HCV RNA are detailed in Supplementary Information 2.

This study conformed to the ethical guidelines of the Declaration of Helsinki (1975) and was approved by the institutional review board (4–2022–0295). The written informed consent was waived due to the retrospective nature.

Definitions

"Anti-HCV tested by alert" was defined as patients who were prescribed and tested for HCV antibody after the alert was triggered before admission. Patients who required hepatology consultation" were defined as those confirmed positive results for HCV antibodies without experiences of previous HCV RNA test results or achieving sustained virologic response for HCV infection using interferon-based therapy or DAAs. Patients who "failed to linkage" were defined as those who required hepatology consultation but had not been referred to a hepatologist or undergone HCV RNA testing. The verification of HCV RNA results was not conducted in this study because it was beyond the scope of this system.

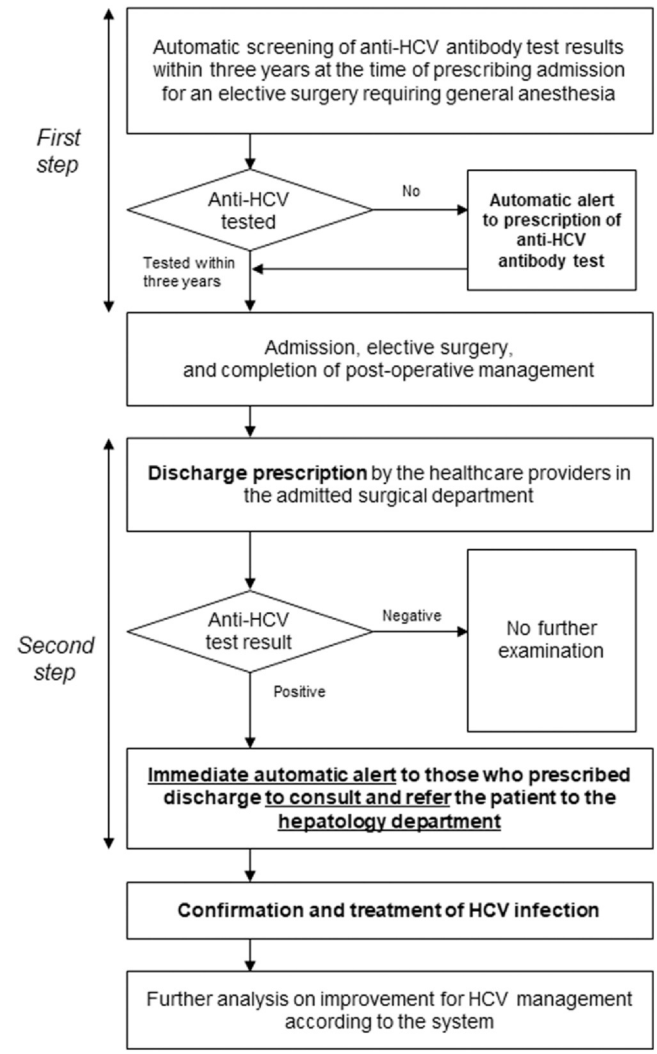

Fig. 1. Flow chart of the EMR-based automatic alert system. EMR, electronic medical record; HCV, Hepatitis C virus.

Surgery department classification

Surgery departments were classified into four groups: group A, hepatobiliary and transplant surgery; group B, other general surgery, pediatric surgery (surgery by pediatric surgeon on patients of age ≥19 years), and obstetrics and gynecology; group C, cardiothoracic surgery, neurosurgery, and orthopedic surgery; and group D, other surgery departments including ear, neck, and throat surgery, oral and maxillofacial surgery, plastic surgery, urology, ophthalmology, and dermatology [8]. Hepatobiliary and transplant surgeries were classified with the expectation of a high awareness of HCV infection in a previous study, whereas the others were classified considering the major disease groups and the number of surgeries handled by each surgery department [8].

Statistical analysis

Data are provided as median with interquartile range (IQR) or number with percentage, as appropriate. The significance of the

Table 1
Comparison between the characteristics of the study population before and after the implementation of the automatic alert system.

Variables	Before automatic system implementation			After automatic system implementation			P value**
	Anti HCV tested	Anti HCV not tested	P value*	Anti HCV tested	Anti HCV not tested	P value*	
HCV antibody tested	106,854 (82.8)	22,211 (17.2)	-	73,834 (96.8)	2476 (3.2)	-	< 0.001
Demographic variables							
Age, year	55.2 (41.8–65.9)	55.7 (40.5–67.0)	0.323	56.8 (42.9–67.1)	57.0 (40.5–68.1)	0.522	< 0.001
Male sex	45,448 (42.5)	10,482 (47.2)	< 0.001	30,667 (41.5)	1233 (49.8)	< 0.001	< 0.001
Body mass index, kg/m^2	23.8 (21.6–26.1)	23.6 (21.5–25.9)	< 0.001	23.9 (21.6–26.4)	23.3 (21.1–25.9)	< 0.001	< 0.001
Hypertension	24,249 (22.7)	4366 (19.7)	< 0.001	16,150 (21.9)	444 (17.9)	< 0.001	< 0.001
Diabetes mellitus	15,713 (14.7)	2781 (12.5)	< 0.001	11,219 (15.2)	309 (12.5)	< 0.001	0.004
Liver cirrhosis	1179 (1.1)	96 (0.4)	< 0.001	907 (1.2)	17 (0.7)	0.02	0.015
Laboratory variables							
Hemoglobin, g/dL	13.5 (12.5–14.6)	13.6 (12.5–14.7)	< 0.001	13.4 (12.4–14.5)	13.2 (11.9–14.4)	< 0.001	< 0.001
Platelet count, 10^9/L	247.0 (208.0–292.0)	248.0 (210.0–293.0)	< 0.001	250.0 (209.0–296.0)	259.0 (212.5–310.0)	< 0.001	< 0.001
Serum albumin, g/dL	4.5 (4.3–4.7)	4.4 (4.2–4.7)	< 0.001	4.5 (4.3–4.7)	4.5 (4.1–4.7)	< 0.001	< 0.001
Total bilirubin, mg/dL	0.6 (0.4–0.8)	0.6 (0.4–0.8)	< 0.001	0.6 (0.5–0.8)	0.6 (0.4–0.8)	0.053	< 0.001
AST, IU/L	20.0 (16.0–25.0)	20.0 (16.0–24.0)	< 0.001	22.0 (18.0–27.0)	21.0 (17.0–27.0)	0.009	< 0.001
ALT, IU/L	17.0 (13.0–25.0)	17.0 (12.0–25.0)	< 0.001	19.0 (13.0–28.0)	18.0 (12.0–27.0)	< 0.001	< 0.001
Blood urea nitrogen, mg/dL	13.8 (11.1–17.2)	13.8 (11.1–17.0)	0.297	14.4 (11.6–17.9)	13.7 (11.1–17.2)	< 0.001	< 0.001
Creatinine, mg/dL	0.8 (0.6–0.9)	0.8 (0.6–0.9)	< 0.001	0.8 (0.6–0.9)	0.8 (0.6–0.9)	0.785	< 0.001
Prothrombin time, INR	1.0 (0.9–1.0)	1.0 (0.9–1.0)	< 0.001	0.9 (0.9–1.0)	1.0 (0.9–1.0)	< 0.001	< 0.001
Positive for HCV antibody	851 (0.8)	-	-	444 (0.6)	-	-	< 0.001
Surgery department			< 0.001			< 0.001	< 0.001
Hepatobiliary and transplant	6512 (6.1)	2816 (12.7)		5277 (7.1)	604 (24.4)		
Other GS, pediatric†, and OBGY	39,800 (37.2)	7127 (32.1)		26,527 (35.9)	1304 (52.7)		
CS, NS, and OS	29,592 (27.7)	8094 (36.4)		23,804 (32.2)	308 (12.4)		
Others‡	30,950 (29.0)	4174 (18.8)		18,226 (24.7)	260 (10.5)		

Values are expressed as number (percentage) or median (interquartile range).
†Surgery on adult patients (age ≥19 years) performed by pediatric surgeons.
‡Ear, neck, and throat surgery, oral and maxillofacial surgery, plastic surgery, urology, ophthalmology, and dermatology.
HCV, Hepatitis C virus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; GS, general surgery; OBGY, obstetrics and gynecology; CS, cardiothoracic surgery; NS, neurosurgery; OS, orthopedic surgery.
* Comparison between HCV antibody-tested and not-tested patients.
** Comparison between HCV antibody-tested patients before and after installation of the automatic alert system.

differences between variables was evaluated using Student's *t*-test or Mann–Whitney *U* test (continuous variables) and chi-squared or Fisher's exact test (categorical variables). Univariate and multivariate logistic regression analyses were used to analyze the association between the linkage failure and risk factors and to calculate their odds ratios (ORs) with 95 % confidence intervals (CI). All statistical analyses were performed using R package (Version 4.2.3, http://cran.r-project.org/). Two-sided *P*-values of < 0.05 were considered to indicate the statistical significance.

Results

HCV antibody testing for patients undergoing surgery

As a *first step*, 129,065 patients between 2016 and 2020 (*Control group*) were included for the comparison with 76,310 patients who were scheduled for elective surgery after the Alert system implementation (*Test group*) (Table 1). The rate of testing HCV antibody significantly improved such that almost all the patients were tested for HCV antibody after the system implementation (82.8–96.8 %, $P < 0.001$). Patients testing HCV antibodies included more women and those who had hypertension, diabetes mellitus, and cirrhosis compared to those who did not, regardless of the system implementation (all $P < 0.05$). The positive rate of HCV antibody testing was 0.8 % (n = 851) and 0.6 % (n = 444) before and after the system implementation, respectively ($P < 0.001$).

Comparison between patients who were alerted and not alerted

The system alerted 12,871 (16.9 %) patients among 76,310 patients in the *Test group* (Supplementary figure 1). The alerted patients tended to be older (median 60.9 vs. 55.9 years) and comprised more men (45.5 % vs. 41.1 %) (all $P < 0.001$). The prevalence of both diabetes and cirrhosis differed significantly between groups (both $P < 0.05$). Out of 12,871 (16.9 %) patients who were alerted to order HCV antibody testing, 12,048 (93.6 %) underwent HCV antibody testing. Of the 63,439 non-alerted patients, 1653 (2.6 %) were not tested for HCV antibody; however, the reason they were not alerted is unknown (Supplementary table 1).

Comparison between patients tested for HCV antibodies before and after the alert

Among 73,834 patients who tested for HCV antibodies, the system alerted 12,048 (16.3 %) patients, of whom 5136 (42.6 %) and 6912 (57.4 %) were prescribed HCV antibody tests before and after the alert, respectively (Supplementary figure 1). Patients who were tested by alert tended to be older (median 62.0 vs. 56.1 years) and male (48.0 % vs. 40.9 %), and had slightly higher prevalence of hypertension (23.4 % vs. 21.7 %), diabetes mellitus (17.5 % vs. 15.0 %), cirrhosis (1.8 % vs. 1.2 %), and positive rate for anti-HCV testing (0.8 % vs. 0.6 %) compared with those who were tested not by alert (all $P < 0.05$) (Supplementary table 2).

Comparison between patients with prescribed HCV antibody test before and after the alert

Among 12,871 alerted patients, HCV antibody test was prescribed to 6935 (53.9 %) patients after alert, in whom HCV antibody testing rate was significantly higher than those before alert (99.7 % vs. 86.5 %, $P < 0.001$) (Supplementary table 3). Similarly, by the surgery department group, the testing rate was significantly higher in those prescribed by alert, especially in group A (99.3 % vs. 53.8 %) and B (99.7 % vs. 67.6 %) (all $P < 0.001$) (Supplementary table 4). Patients in group A showed higher positive rate for HCV antibody test (1.4 %) than those in the other groups (0.6 %).

Table 2
Comparisons between patients who were positive for HCV antibody at discharge before and after the automatic alert system implementation.

Variables	Before implementation (n = 851)	After implementation (n = 463)	*P* value
Demographic variables			
Age, year	65.3 (56.9–73.8)	65.0 (57.0–76.0)	0.340
Male sex	407 (47.8)	240 (51.8)	0.183
Body mass index, kg/m^2	23.7 (21.8–26.1)	24.2 (22.0–26.7)	0.020
Hypertension	324 (38.1)	245 (52.9)	< 0.001
Diabetes mellitus	216 (25.4)	139 (30.0)	0.081
Liver cirrhosis	93 (10.9)	56 (12.1)	0.585
Laboratory variables			
Hemoglobin, g/dL	13.3 (12.0–14.4)	11.4 (9.9–13.1)	< 0.001
Platelet count, 10^9/L	207.0 (158.0–253.0)	196.0 (154.5–246.5)	0.121
Serum albumin, g/dL	4.3 (4.0–4.6)	3.8 (3.4–4.3)	< 0.001
Total bilirubin, mg/dL	0.6 (0.4–0.8)	0.6 (0.5–0.9)	0.138
AST, IU/L	24.0 (19.0–33.0)	24.0 (19.0–33.0)	0.604
ALT, IU/L	20.0 (14.0–29.0)	19.0 (12.0–27.0)	0.047
Blood urea nitrogen, mg/dL	15.3 (12.4–19.2)	15.0 (11.9–19.3)	0.360
Creatinine, mg/dL	0.8 (0.7–0.9)	0.8 (0.6–0.9)	0.582
Prothrombin time, INR	1.0 (0.9–1.0)	1.0 (0.9–1.0)	0.020
Surgery department			0.040
Hepatobiliary and transplant	123 (14.5)	69 (14.9)	
Other GS, pediatric†, and OBGY	211 (24.8)	90 (19.4)	
CS, NS, and OS	288 (33.8)	189 (40.8)	
Others‡	229 (26.9)	115 (24.8)	
Hospitalized days	7.0 (4.0–12,0)	6.0 (4.0–10.0)	0.005
Previous consultation to hepatology	-	61 (13.2)	-
Consultation after alert	-	29 (6.3)	-
Total consultation to hepatology	-	90 (19.4)	-
Consultation required among alerted	-	275 (59.4)	-
Consulted among required	-	42 (15.3)	-
Previous HCV RNA tested	503 (59.1)	230 (49.7)	0.001
Previous HCV RNA positivity	148 (29.4)	117 (50.8)	< 0.001

Values are expressed as number (percentage) or median (interquartile range).
†Surgery on adult patients (age ≥19 years) performed by pediatric surgeons.
‡Ear, neck, and throat surgery, oral and maxillofacial surgery, plastic surgery, urology, ophthalmology, and dermatology.
HCV, Hepatitis C virus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; GS, general surgery; OBGY, obstetrics and gynecology; CS, cardiothoracic surgery; NS, neurosurgery; OS, orthopedic surgery

Comparison between patients testing positive for HCV antibody after surgery before and after implementing Alert system

As the *second step*, we reviewed patients who tested positive for HCV antibody testing before and after the implementation of the Alert system. At the time of the discharge prescription, the system alerted 463 patients testing positive for HCV antibody in the *Test group*, including 19 patients admitted before the system implementation (Table 2). These patients had a significantly higher prevalence of hypertension (52.9 % vs. 38.1 %), lower median levels of hemoglobin (11.4 vs. 13.3 g/dL) and serum albumin (3.8 vs. 4.3 g/dL) at discharge, and shorter length of hospitalization (6.0 vs. 7.0 d), compared to 851 patients who tested positive for HCV antibody in the *Control group* (all $P < 0.05$). Previous HCV RNA testing rate before admission was lower after the implementation of Alert system (49.7 % vs. 59.1 %, $P = 0.001$); however, positive rate for previously tested HCV RNA before admission was higher after implementation (50.8 % vs. 29.4 %, $P < 0.001$).

Consultation and referral for patients testing positive for HCV antibody after surgery

Out of 463 alerted patients in the *Test group*, 90 (19.4 %) and 29 (6.3 %) patients consulted to hepatology department during and after the alert, respectively. The consultation was required in 275 (59.4 %) patients; however, only 42 (15.3 %) patients consulted during the admission period (Table 2). The quarterly consultation rate varied (10.9 %–38.7 % in total, and 0.0 %–19.4 % after alert) without a clear trend in the increase in consultation rate over time after the implementation (Fig. 2). Among the surgery department groups, group A showed the highest previous HCV RNA testing rate (79.7 %) and the lowest failure rate to linkage (50.0 % vs. 85.0–93.2 % in other groups) (Supplementary table 5). When compared to 373 non-consulted patients, 90 consulted patients showed significantly lower median value of hemoglobin (10.9 vs. 11.6 g/dL) and serum albumin (3.6 vs. 3.9 g/dL), longer duration of hospitalization (9.0 vs. 5.0 d), and higher previous testing rate for HCV RNA (64.4 vs. 46.1 %) (all $P < 0.05$) (Table 3). Among consulted, the duration of hospitalization was significantly longer in those who consulted before alert (11.0 vs. 6.0 d, $P = 0.005$) (Supplementary table 6).

Factors contributing to the linkage failure

Univariate logistic regression analysis revealed the potential factors related to the linkage failure after alert for positive testing for HCV antibody, such as hypertension, diabetes mellitus, non-cirrhosis, duration of hospitalization, and surgery department (groups B–D vs. group A). Multivariate analyses revealed the independent risk factors including the patients in groups B–D (vs. group A) with higher risk (OR=5.940, 95 % CI, 3.080–12.410, $P < 0.001$) and the duration of hospitalization that was inversely associated (OR=0.980, 95 % CI, 0.950–0.990, $P = 0.012$) (Table 4).

Discussion

Several methods have been proposed to enhance the HCV-care cascade, including an electronic notification system that automatically alerts upon recognizing HCV antibody positivity [13], a reflex testing that automatically performs HCV RNA and genotype tests for patients testing positive for HCV antibody [14,15], and a call-back strategy that involves directly contacting the identified patients [16]. In addition to the privacy issues, we considered the

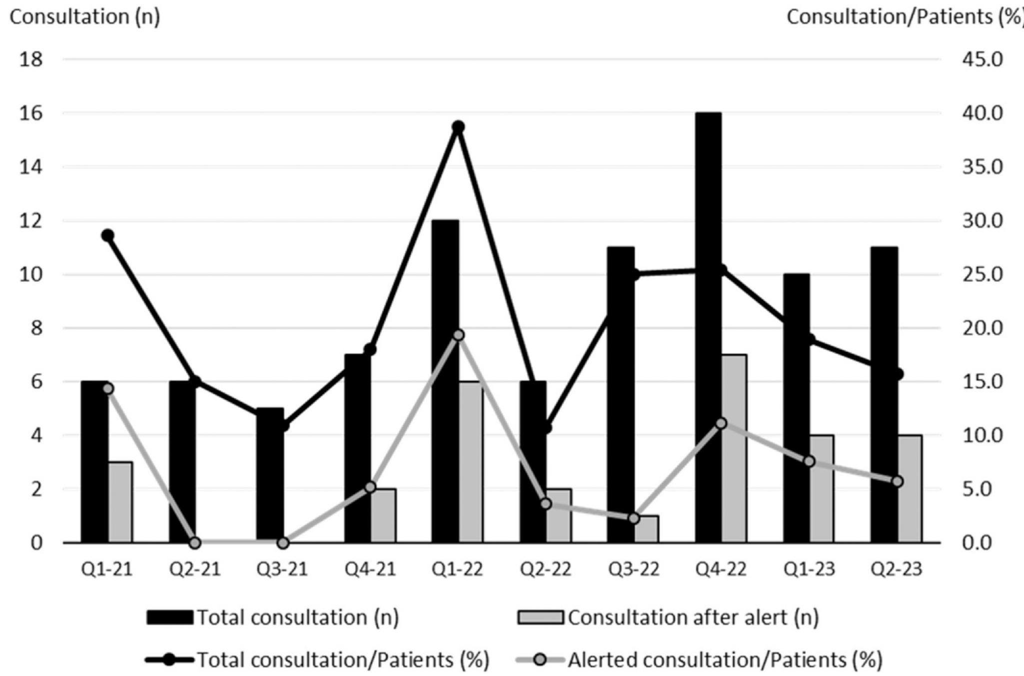

Fig. 2. Hepatology consultations among patients with an alert for positive testing for HCV antibody from the first quarter of 2021 (Q1–21) to the second quarter of 2023 (Q2–23) after the automatic system implementation.

pitfalls in a tertiary medical center in South Korea such as potential cost issues associated with linkage failure after reflex testing and practical difficulties related to direct call-backs that should be performed by the primary surgeon. Therefore, we developed the Alert system that could be applied without any specific limitations to our institution's system in 2021.

We investigated the impact of implementing an EMR-based automatic alert system for HCV screening and linkage to care for patients undergoing elective surgery. Following implementation, the *first step* of our Alert system significantly increased the HCV screening rate within 3 years in patients undergoing surgery (82.8–96.8 %, P < 0.001). The positive rate of HCV antibody testing rate decreased (0.8–0.6 %) after implementation, while the positive rate was similar with those previously reported in recent Korean studies (0.30–0.78 %). [5,17,18] However, only 42 (15.3 %) out of 275 (59.4 %) patients who needed to be linked to care cascade were referred to the hepatologists, and the *second step* of our Alert system resulted in only 29 (32.2 %) hepatology consultations initiated by alert out of a total 90 hepatology consultation (19.4 %). Therefore, in our study, the Alert system demonstrated limited effectiveness in linking HCV antibody-positive patients identified during the surgical process to the care cascade.

Our study has several important clinical implications. First, after Alert system implementation, almost all (96.8 %) patients scheduled for surgery in the outpatient clinic underwent HCV screening within 3 years. In South Korea, HCV screening is covered by KNHIS reimbursement only in situations related to liver abnormalities, blood transfusions, and organ transplantation, and national health examinations do not yet include HCV screening despite the proven cost effectiveness of the universal HCV screening program [19]. Excluding individual health check-ups, preoperative HCV screening might be the only opportunity to identify early and asymptomatic HCV infection in South Korea. The recent KNHIS data showed a linkage to care rate of 78.2 % and a treatment rate of 58.1 % for new 8810 HCV RNA-positive cases in 2019 [20], of which treatment rate was higher than 45 % that was reported in a global modeling study [21]. This suggests that treatment strategies using DAAs for identified HCV RNA-positive patients are being effectively implemented in South Korea, and it also signifies that the identification of undiagnosed patients will be an ongoing challenge for HCV elimination. Therefore, even if patients in *Control group* also showed a high HCV screening rate (82.8 %), the fact that 12,048 patients (13.3 %) in *Test group* newly underwent HCV screening associated with alerts demonstrates the significant impact of our *first step* of the Alert system.

Second, the linkage to the HCV RNA confirmation cascade for many patients testing positive for HCV antibody is an ongoing necessity. In the *second step*, even if the lower proportion of patients in the *Test group* had previously undergone HCV RNA testing (49.7 % vs. 59.1 % in the *Control group*), the positive rate for the previous HCV RNA test was higher in the *Test group* (50.8 % vs. 29.4 % in the *Control group*), although its reason is not clear. Furthermore, more than a half (n = 275, 59.4 %) of the alerted patients in the *Test group* still required consultation to hepatologist due to lack of a previous nondetectable HCV RNA result or a successful treatment history for HCV infection. Despite the recently reported higher treatment rates (58.1 %) in South Korea [20], these findings suggest that a significant proportion of asymptomatic HCV infection remains undetected and should be addressed in the care cascade.

Third, the disappointing rate of linkage-to-care (15.3 %) among patients who tested positive for HCV antibody suggests that the EMR-based automatic alert system had a limited impact on raising awareness of the HCV care cascade among healthcare providers in surgical departments. Providers in inpatient surgical departments initiated fewer hepatology consultations after the alert (29 patients) than before it (61 patients). Both patients with a longer duration of hospitalization and those in hepatobiliary and transplant surgery departments, expected to have greater awareness of infection control, had more opportunities for inpatient hepatology consultation. These findings suggest the proactive awareness and clinical judgment of inpatient healthcare providers, rather than the alert itself, played a more substantial role in facilitating the HCV care cascade. While the Alert system was effective in identifying patients with potential HCV infection, it was insufficient in facilitating actual linkage to care when relying solely on passive education and guidance. Several factors may have contributed, such as a lack of understanding of the clinical implications of anti-HCV positivity, a

Table 3
Comparisons between patients with positive testing for HCV antibody who consulted hepatologists and those who did not.

Variables	Non-consulted (n = 373)	Consulted (n = 90)	*P* value
Demographic variables			
Age, year	65.0 (57.0–76.0)	65.0 (58.0–75.0)	0.978
Male sex	190 (50.9)	50 (55.6)	0.503
Body mass index, kg/m^2	24.4 (22.1–26.9)	23.9 (21.9–26.2)	0.307
Hypertension	194 (52.0)	51 (56.7)	0.499
Diabetes mellitus	106 (28.4)	33 (36.7)	0.160
Liver cirrhosis	40 (10.7)	16 (17.8)	0.097
Laboratory variables			
Hemoglobin, g/dL	11.6 (10.0–13.2)	10.9 (9.5–12.1)	0.010
Platelet count, 10^9/L	194.0 (157.0–243.0)	209.0 (148.0–250.0)	0.481
Serum albumin, g/dL	3.9 (3.5–4.4)	3.6 (3.3–4.0)	< 0.001
Total bilirubin, mg/dL	0.7 (0.5–0.9)	0.6 (0.4–0.7)	0.087
AST, IU/L	23.0 (18.0–31.0)	29.5 (20.0–42.0)	0.004
ALT, IU/L	19.0 (12.0–27.0)	20.0 (13.0–35.0)	0.130
Blood urea nitrogen, mg/dL	15.0 (12.0–19.2)	14.5 (11.6–19.4)	0.516
Creatinine, mg/dL	0.8 (0.6–0.9)	0.8 (0.6–1.0)	0.671
Prothrombin time, INR	1.0 (0.9–1.0)	1.0 (0.9–1.0)	0.067
Surgery department			< 0.001
Hepatobiliary and transplant	38 (10.2)	31 (34.4)	
Other GS, pediatric†, and OBGY	79 (21.2)	11 (12.2)	
CS, NS, and OS	153 (41.0)	36 (40.0)	
Others‡	103 (27.6)	12 (13.3)	
Hospitalized days	5.0 (3.0–9.0)	9.0 (5.0–14.0)	0.005
Previous HCV RNA result	172 (46.1)	58 (64.4)	0.003
Previous HCV RNA positivity	87 (50.6)	30 (51.7)	> 0.999

Values are expressed as number (percentage) or median (interquartile range).
†Surgery on adult patients (age ≥19 years) performed by pediatric surgeons
‡Ear, neck, and throat surgery, oral and maxillofacial surgery, plastic surgery, urology, ophthalmology, and dermatology.
HCV, Hepatitis C virus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; GS, general surgery; OBGY, obstetrics and gynecology; CS, cardiothoracic surgery; NS, neurosurgery; OS, orthopedic surgery.

perception that the EMR consultation process was overly cumbersome, or competing clinical demands that limited attention to the alert. Specifically, the design of the Alert system included pop-up menus for consultation requests and outpatient appointment scheduling, requiring healthcare providers to complete these steps manually. These steps were necessary to respect patient autonomy and comply with legal and ethical requirements for protecting patient privacy and obtaining informed consent. However, these additional steps may have increased the administrative burden on inpatient healthcare providers. Combined with limited awareness and time constraints during perioperative care, these factors may discourage them from completing the referral and follow-up processes, ultimately contributing to the low linkage-to-care rates observed in our study. However, the limited efficacy of the EMR-based automatic alert system observed in surgical departments may not be applicable to other settings. Recent studies have suggested that electronic alert systems within the HCV-care cascade yield successful or improved linkage to care for HCV infection (42.9–94.2 %) when applied to patients from emergency departments or departments of internal medicine [13,14,22,23]. These findings underscore the limitations of passive alert systems in surgical settings.

Fourth, additional assertive measures, such as reflex testing or a call-back system, may be required in the HCV-care cascade from healthcare providers in surgical departments who are less familiar with viral Hepatitis. Reflex testing involves automatically performing an HCV RNA test, without an additional physician order, following a positive anti-HCV antibody result, using a single-visit sample [24]. Successful scaling up of the in-hospital care cascade in Taiwan has been reported, and the application of both reflex testing and a later call-back strategy successfully improved HCV RNA testing rate (23.3–100 %) and treatment rate (27.8–73.9 %) [25]. The feasibility of reflex testing and call-back strategies in a medical institution, as demonstrated in Taiwan, depends not only on substantial financial and human resources, but also on strong government commitment to combating the national disease burden of Hepatitis B and C [26]. A recent Korean study using an in-hospital reflex testing model also showed significant improvement in HCV RNA testing rates (51.0–95.6 %) and referral rates (57.1–81.1 %) [27]. Successful implementation and maintenance of reflex-testing and call-back systems require legislative support to ensure that infection-

Table 4
Independent risk factors for linkage failure after alert for positive testing for HCV antibody.

Variables	Univariate analysis		Multivariate analysis		Multivariate analysis	
	Odds ratio (95 % CI)	*P* value	Odds ratio (95 % CI)	*P* value	Odds ratio (95 % CI)	*P* value
Age	1.010 (1.000–1.030)	0.149				
Male sex	0.850 (0.590–1.220)	0.374				
Body mass index, kg/m^2	1.000 (0.950–1.050)	0.887				
Hypertension	0.700 (0.480–1.010)	0.056	0.860 (0.570–1.300)	0.482	0.780 (0.520–1.170)	0.225
Diabetes mellitus	0.580 (0.390–0.870)	0.009	0.730 (0.470–1.140)	0.163	0.690 (0.450–1.070)	0.100
Non-cirrhosis	2.160 (1.220–3.950)	0.010	1.790 (0.960–3.390)	0.071	1.940 (1.060–3.650)	0.034
Hemoglobin, g/dL	1.060 (0.980–1.160)	0.163				
Platelet count, 10^9/L	1.000 (1.000–1.000)	0.173				
Serum albumin, g/dL	1.070 (0.770–1.490)	0.690				
Total bilirubin, mg/dL	1.340 (0.860–2.140)	0.200				
AST, IU/L	0.990 (0.990–1.000)	0.083	1.000 (0.990–1.000)	0.293	0.990 (0.990–1.000)	0.168
ALT, IU/L	1.000 (0.990–1.000)	0.215				
Blood urea nitrogen, mg/dL	0.980 (0.960–1.000)	0.058	0.980 (0.960–1.000)	0.094	0.980 (0.960–1.000)	0.082
Creatinine, mg/dL	0.940 (0.810–1.080)	0.418				
Prothrombin time, INR	2.220 (0.560–10.020)	0.270				
Hospitalized days (d)	0.970 (0.940–0.990)	0.003	0.980 (0.950–0.990)	0.012	0.970 (0.950–0.990)	0.005
Groups B–D (vs. Group A)	6.810 (3.600–14.040)	< 0.001	5.940 (3.080–12.410)	< 0.001	-	-
Groups C–D (vs. Groups A–B)	1.720 (1.170–2.540)	0.006	-	-	1.930 (1.280–2.920)	0.002

Values are expressed as number (percentage) or median (interquartile range).
Group A, Hepatobiliary and transplant surgery.
Group B, other general surgery, pediatric surgery (on age ≥19 years), obstetrics and gynecology.
Group C, cardiothoracic surgery, neurosurgery, and orthopedic surgery.
Group D, ear, neck, and throat surgery, oral and maxillofacial surgery, plastic surgery, urology, ophthalmology, and dermatology.
HCV, Hepatitis C virus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; CI, confidence interval.

related data are accessed and acted on by non-consulted departments for infection-control purposes. Moreover, public education is necessary to enhance understanding of the importance of hospital follow-up and the potential costs. Since 2025, South Korea has implemented nationwide anti-HCV antibody screening for all individuals aged 56 as part of the national health checkup program. For those who test positive, the government began subsidizing the cost of HCV-RNA testing at primary-care clinics, which is expected to contribute to future HCV elimination efforts.

Several limitations exist. First, this study did not investigate the result of HCV RNA tests and subsequent treatment since the scope of the Alert system was limited to successfully linking the patients to hepatologists. Second, the results from our single center study should not be generalized to the surgical departments of other medical institutions. Third, our study eventually failed to improve linkage to care cascade for undiagnosed patients with HCV infection who underwent elective surgery. Nonetheless, these findings provide valuable insights for implementing an improved system for the uncovered patients. We will initiate call-back procedures for the recently identified patients.

Conclusion

The EMR-based automatic alert system effectively increased HCV screening for patients undergoing elective surgery before admission. However, it could not link them to care cascade in surgery departments. Combining more proactive approaches would be beneficial, such as reflex testing or a call-back strategy.

CRediT authorship contribution statement

Conceptualization, JS Lee and SU Kim; data curation, JS Lee and SU Kim; formal analysis, JS Lee and SU Kim; funding acquisition, SU Kim; investigation, JS Lee and SU Kim; methodology, JS Lee, HS Chun, and SU Kim; project administration, SU Kim; resources, JS Lee, HW Lee, MN Kim, BK Kim, DY Kim, SH Ahn, and SU Kim; writing-original draft preparation, JS Lee; writing-review and editing, JS Lee, HS Chun, HW Lee, MN Kim, BK Kim, DY Kim, SH Ahn, and SU Kim; supervision, SU Kim; validation, JS Lee; visualization, JS Lee. All authors have read and agreed to the published version of the manuscript.

Ethical approval statement

This study conformed to the ethical guidelines of the Declaration of Helsinki (1975) and was approved by the institutional review board (4–2022–0295). The need for written informed consent was waived due to the retrospective nature of the study.

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Declaration of Competing Interest

All authors have no conflict of interests.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2025.103076.

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