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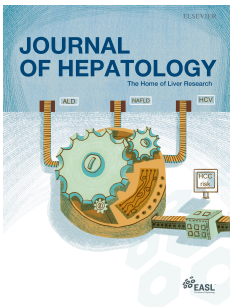

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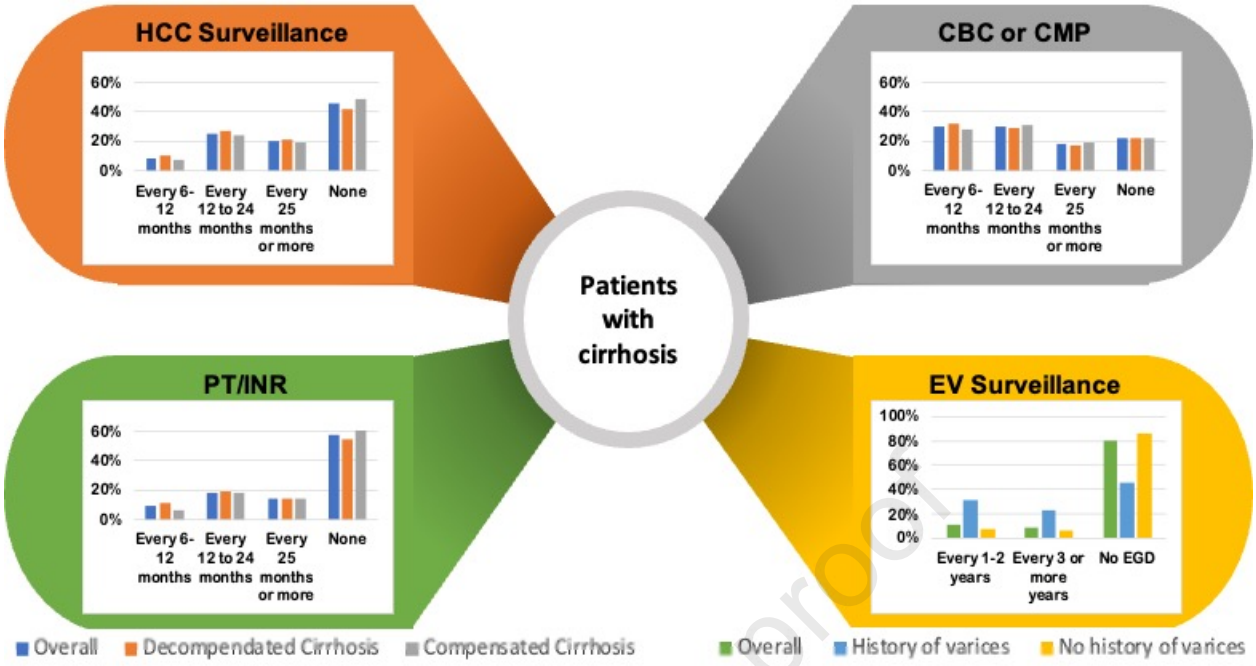

Surveillance of patients with cirrhosis remains suboptimal in the United States

Short title: Status of Cirrhosis Quality Care Metrics

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Key Words: Truven Health MarketScan Research Database; hepatocellular carcinoma surveillance; oesophageal varices surveillance; health monitoring; quality improvement

Data availability statement

The full data are not publicly available due to limitations posed by the purchase contract between Stanford University and the Truven Health MarketScan Research Database.

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Abstract (260/275 words)

Background & Aims: Regular monitoring/surveillance for liver complications is crucial in the management of patients with cirrhosis to reduce morbidity and mortality. Recommendations from professional societies are available but adherence is not well studied, especially outside of academic centers. We aimed to determine the frequencies and factors associated with laboratory monitoring, hepatocellular carcinoma (HCC) and esophageal varices (EV) surveillance in patients with cirrhosis.

Methods: We identified 82,427 patients with cirrhosis (43,280 compensated and 39,147 decompensated) from the Truven Health MarketScan Research Database®, 2007-2016. We calculated the proportion of patients with cirrhosis with various frequencies of procedures/testing for laboratory (complete blood count, comprehensive metabolic panel, and prothrombin time), HCC and EV surveillance. We also used multivariable logistic regression to determine factors associated with having procedures.

Results: The proportions of patients undergoing HCC surveillance (8.78%), laboratory testing (29.72%) at least every 6-12 months, or EV surveillance (10.6%) at least every 1-2 years were suboptimal. The majority did not have HCC (45.4%) or EV (80.3%) surveillance during the entire study period. On multivariable regression, age 41-55 (vs. <41) years, PPO (vs. HMO) insurance plan, specialist care (vs. primary care and other specialties), diagnosis between 2013-2016 (vs. 2007-2009), decompensated (vs. compensated) cirrhosis, NAFLD (vs. viral hepatitis), and higher Charlson's comorbidity index were associated with significantly higher odds of undergoing procedures/testing every 6-12 months and EV surveillance every 1-2 years.

Conclusions: Despite having modest improvement in the more recent years, routine monitoring and surveillance for patients with cirrhosis is suboptimal. Further efforts including provider

awareness, patient education, and system/incentive-based quality improvement measures are urgently needed.

Lay summary

Patients with cirrhosis should undergo health monitoring for liver complications to achieve early detection and treatment. In a large nationwide cohort of 82,427 patients with cirrhosis in the United States, we found a low rate of adherence (well less than half) to routine blood test monitoring and surveillance for liver cancer and esophageal varices (swollen blood vessels in the abdomen that could lead to fatal bleeding). Adherence has increased in the recent years, but much more improvement is needed.

Introduction

Cirrhosis is considered the common end pathway of most chronic liver diseases and can carry a high mortality rate due to its associated complications (e.g. ascites, hepatic encephalopathy, esophageal varices, and hepatocellular carcinoma [HCC]).[1-3] Globally, cirrhosis is the 11th most common cause of death, while it is the 10th leading cause of death in the United States (U.S.).[4],[5]

Between 1999 and 2016, the U.S. annual deaths from cirrhosis increased by 65%, reaching 34,174 cirrhosis related annual deaths by 2016.[6] Cirrhosis is also associated with substantial health and economic burdens as a result of the aforementioned morbidities which lead to increased number of hospital admissions and readmissions within 30 days.[7, 8]

As a result, several practice guidelines and quality measures have been developed by various professional societies to avert many of the complications associated with cirrhosis not the least of which includes meticulous surveillance for HCC, esophageal varices, and general patient well-being with regular clinical and laboratory evaluation.[9-14] However, given the high risk of sarcopenia, ascites, and hepatic encephalopathy, which affect mobility and access to care, it is challenging to engage patients with cirrhosis. Furthermore, the recent shift to value-based health care, defined as achieving desired outcomes relative to the cost of care for patients, poses an urgent need to measure and improve cirrhosis care quality. This is especially important in light of a recent meta-analyses which found that the quality of care for patients with cirrhosis with regards to HCC surveillance and inpatient care of decompensated patients with cirrhosis was poor.[15-17] Wolf et al. reported a pooled HCC surveillance rate of 24%, though the data may be heterogeneous and likely skewed by the surveillance rate from subspecialty care settings.[18-21] In fact, in subgroup analysis of population-based studies, the pooled rate of HCC surveillance

was only 9.8%, but this data is also likely heterogeneous with surveillance rates of individual studies ranged from 1.1% to 50%, limiting its conclusion.

Furthermore, current coronavirus-19 (COVID-19) pandemic drastically reduced the number of liver patient visits and monitoring tests compared to the same month in prior years at institutions from the US, Singapore, and Japan.[22] Toyoda et al. reported an almost 40% decrease in HCC and/or cirrhosis clinic encounter. The negative effect of COVID-19 on medical care is also expected to be long-lasting.[23]

Therefore, to inform practice with the current status of monitoring and surveillance in patients with cirrhosis, we aimed to characterize the frequencies and factors associated with standard best practice to include key measures such as routine laboratory monitoring, HCC and esophageal varices (EV) surveillance in a large cohort of privately insured patients with cirrhosis in the U.S.

Methods

Data source

We conducted a retrospective cohort study using an administrative claims database, Truven Health MarketScan Research Database® (Truven database), to identify patients with cirrhosis between 2007 and 2016. Collating data from more than 100 health plans, employers, government agencies, and public organizations, the database contains person-level data for diagnoses, procedures, and dispensed medications across all settings, including physician consultation, hospitalization, health plan, provider type, and region. Data were provided by the Population Health Science Center at Stanford University, California, U.S. The Stanford University Medical Center's the Institutional Review Board approved this study.

Definitions

Adult patients (aged ≥18 years) with cirrhosis were identified using the international classification of diseases, Ninth and Tenth revision, clinical modification/procedure coding system (ICD-9 & 10-CM/PCS). To maximize the positive predictive value for patient selection, the patients had to have at least one inpatient or two outpatient diagnoses of cirrhosis or complications of cirrhosis such as hepatic encephalopathy and/or ascites in the setting of a chronic liver disease (**Supplementary Table 1**). The first date of cirrhosis diagnosis was assigned as the index date. We also required at least one year of insurance enrolment after the index date and insurance coverage for at least 60 days during each six-month period during the study follow-up. We excluded patients who had a diagnosis of orthotopic liver transplantation (OLT) or HCC before the index date. For patients who had diagnoses of both compensated and decompensated cirrhosis during study period, we set the index date on the first date of having decompensated cirrhosis and disregarded the prior period with compensated cirrhosis to avoid misclassification bias. Patients were censored at the date for OLT, HCC, the end of enrolment, or December 31, 2016, whichever occurred first.

For demographic characteristics, we categorized insurance type into health maintenance organization (HMO), preferred provider organization (PPO), and other. Patients who choose HMO insurance plan are required to choose medical providers from a list of contracted "in-network" providers assigned for their coverage area. The insured HMO patients also need to have a primary care physician who is a contracted "in network" provider to act as a "gate keeper" and screen for medically necessary indication before ordering a referral to specialist. HMO insurance plan generally has lower monthly insurance premium cost and lower yearly additional out-of-pocket expense for patient. PPO insurance plan, on the other hand, has less restriction than HMO. PPO also usually requires a higher monthly insurance premium as well as co-pay

and other out-of-pocket expense for patients than HMO plan does. However, patients with PPO insurance plan can expect to have more flexibility in their choice of medical care providers and generally do not need approval from their primary care providers or insurance plan to see specialists. It also allows patients to see providers outside the network but with less coverage. We defined the specialty as the first provider whose visit was associated with the diagnosis of cirrhosis. To increase the sensitivity of this definition, we defined primary care providers (PCP) as family medicine, internal medicine, obstetrics or gynecology, and hospital medicine practitioners. Since some patients with viral hepatitis associated cirrhosis may receive specialist care with infectious disease specialist, we defined the specialist group as gastroenterology, hepatology, or infectious disease (GI/ID) practitioners.

To determine the level of illness related to comorbidities, we calculated the Charlson's comorbidity index (CCI) but did not include liver-related diseases to avoid inclusion of overlapping variables in the multivariable models.

Adherence to health monitoring

The primary outcome of this study was frequency of liver testing including (1) abdominal ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI); (2) routine laboratory testing including complete blood count (CBC) and comprehensive metabolic panel (CMP); (3) prothrombin time (PT) and international normalized ratio (INR) as an additional measurement of hepatic function recommended for patients with cirrhosis; and (4) esophagogastroduodenoscopy (EGD) (the ICD-9/10 codes or current procedural terminology (CPT) (**Supplementary Table 2**). We considered imaging alone as measurement for adherence to HCC surveillance since alpha fetoprotein was either not recommended or only optional by various guidelines.[13, 24] All outcomes were stratified by the presence of hepatic

decompensation. For EV surveillance frequency, we further stratified patients by (1) with history of varices, (2) no history of varices.

To avert a false increase in the surveillance rate, we divided the follow up period for each patient into 3-month blocks and measured whether patients received a liver testing/procedure or not during each block (binary outcome). If patients had liver testing or a procedure in a block, that block was considered "covered". For example, if a patient had more than one abdominal imaging performed in a 3-month block, the patient was considered to have testing/procedure during this block. We then calculated number of blocks with testing dividing by the number of blocks for each patient during the follow up period (e.g., 3 blocks with testing out of 5 blocks). We converted this to annual frequency and categorized patients into one of the following 5 groups: no testing, testing at least every 6-12 months, every >12 months to 24 months, and every >24 months. For EV surveillance, we categorized patients into 3 groups: no surveillance, every 1-2 years, and every >2 years.

Statistical Analysis

Baseline characteristics including sex, age, insurance type, provider specialty, year, geographic region, and CCI were summarized by descriptive statistics. We compared categorical variables between patients with compensated cirrhosis and those with decompensated cirrhosis using the chi-square test. We performed multivariable logistic regression to determine factors associated with having testing/procedure at least every 6-12 months compared to having testing/procedure more than every 6-12 months or no testing/procedure. We also determined the factors associated with having EV surveillance at least every 1-2 years. For sensitivity analysis, we required patients to have continuous enrolment in the health plan 1 year after the index date without any gap given that some patients may have gaps of enrolment during follow up period. A

two-tailed *P* value <0.05 was set as the threshold for statistical significance. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

Patient Characteristics

A total of 279,925 patients with diagnoses of cirrhosis were identified during 2007 to 2016 (**Supplementary Figure 1**). After excluding patients aged <18 years, those with history of HCC and OLT before the index date, and those with enrolment period after index date of less than one year, 82,427 patients with cirrhosis were included for the study analysis. The overall mean follow-up time was 29.1±15.3 months. (**Table 1**). There were more males than female patients with cirrhosis, and about half of the cohort was 55 years or older. Patients who were insured under a PPO plan constituted about 60% of the cohort, while those with an HMO plan represented 11.27%. More than half of the patients were seen by GI/ID specialists, followed by PCP and other specialties. Approximately three quarters of patients had CCI of 0 to 2, 17% had a CCI of 3 to 4, and 9% of the patients had a CCI of ≥5.

In the subgroup of patients with decompensated cirrhosis, there was a higher proportion of patients who were older, male, insured with non-HMO and non-PPO, seen by GI/ID, with a higher CCI compared with patients with compensated cirrhosis. **(Table 1)** The incidence of HCC among the included patients was 4.69 per 1000 person-years while it was 12.69 per 1000 person-years for variceal bleeding.

Frequencies and Predictor of Procedures/Testing

HCC surveillance

The proportions of patients who underwent HCC surveillance by imaging (ultrasound, CT scan, and/or MRI) at least once every 6-12, >12-24, and >24 months were 8.78%, 25.32%, and

20.47%, respectively (**Figure 1 A**). Nearly half of patients with cirrhosis had no abdominal imaging during their entire follow up period.

On multivariable analysis, having a PPO (vs. HMO) insurance plan (aOR 1.16, 95% CI 1.06-1.25), being diagnosed in 2013-2016 (vs. 2007-2009) (aOR 1.32, 95% CI 1.28-1.45), having NAFLD (vs. viral hepatitis) (aOR 1.58, 95% CI 1.33-1.88), having decompensated (vs. compensated) cirrhosis (aOR 1.51, 95% CI 1.43-1.59), and having a higher CCI score (3-4 vs. 1: aOR 1.15, 95% CI 1.07-1.23; ≥5 vs. 1: aOR 1.23, 95% CI 1.13-1.35) showed a higher probability of having undergone abdominal imaging at least every 6-12 months (**Table 2**). Being seen by physicians other than a GI/ID specialist, seen in 2010-2012 compared to 2007-2009, and having CCI <1 (vs. 1) showed a negative association.

Routine Laboratory Testing (CBC, CMP)

The proportions of patients who received laboratory tests at least once every 6-12, >12-24, and >24 months were 29.72%, 30.24%, and 18.00%, respectively (**Figure 1 B**). About a quarter of patients had no CBC or CMP during the study period.

Age 41-55 years (vs. 18-40: 1.16, 95% CI 1.10-1.22), having decompensated cirrhosis (aOR 1.17, 95% CI 1.13-1.21), having a higher CCI (score 3 to 4: aOR 1.17, 95% CI 1.12-1.23; score ≥5: aOR 1.37, 95% CI 1.29-1.45; all with score 1-2 as reference), having NAFLD (aOR 1.43, 95% CI 1.27-1.61) and alcohol-associated liver disease (ALD, vs. viral hepatitis, aOR 1.38, 95% CI 1.20-1.58,), and being diagnosed in 2013-2016 vs. 2007-2009 (aOR 1.25, 95% CI 1.20-1.30) were associated with a higher probability of undergoing laboratory testing at least every 6-12 months while having insurance other than an HMO or PPO plan as well as being seen by physicians other than a GI/ID specialist were associated with lower odds of having laboratory testing (**Table 3**).

Monitoring for PT/INR

The proportion of patients with PT and INR tests at least every 6-12, >12-24, and >24 months among patients with cirrhosis was 9.17%, 18.60%, and 14.62% respectively (**Figure 1 C**). Multivariable analysis showed that older age, being diagnosed in recent years, having decompensated cirrhosis, NAFLD and ALD, as well as having higher CCI were associated with higher odds of undergoing PT/INR test at least every 6-12 months while being female and seeing physicians other than GI/ID specialists were associated with lower odds of having PT/INR tests (**Table 4**).

Esophageal Varices Surveillance

The frequencies of EV surveillance for patients with cirrhosis were low, with more than 80% patients not having any endoscopy during study period. When categorized by history of varices, those with varices had EV surveillance at least every 1-2 years and >2 years were 31.1%, and 23.1%, respectively, while they were 7.11%, and 6.71% in those without a history of varices (**Figure 2**).

Having PPO insurance (aOR 1.17, 95% CI 1.08-1.26, vs. HMO), being diagnosed in 2013-2016 vs. 2007-2009 (aOR 1.29, 95% CI 1.22-1.37), being diagnosed with having varices (aOR 4.60, 95% CI 4.36-4.84 vs. no varices), and having higher CCI (score 3 to 4: aOR 1.12, 95% CI 1.05-1.20; score ≥5: aOR 1.17, 95% CI 1.08-1.27; both vs. score 1-2) were associated with higher odds of having endoscopy at least every 1-2 years, while seen by PCP and other specialties (compared to GI/ID specialists) was related with lower odds (**Table 5**).

Sensitivity analysis

In the sensitivity analysis which included only patients with cirrhosis who had a continuous enrolment period of at least 12 months (N = 58,336) (as opposed to patients with 12-month enrollment but with at least 60 days in every 6 months' block), the proportions of each subgroup were similar, except with higher proportion of patients diagnosed in 2013-2016 (46.68%). The frequencies and predictors are generally similar to those of the main analyses (**Supplementary Figures 2-3 and Supplementary Tables 3-7**).

Discussion

Using a nationwide database from 2007 to 2016, we quantified the frequency of laboratory monitoring and imaging/procedural surveillance in privately insured patients with cirrhosis and identified the potential factors that predicted adherence to the current recommendations on cirrhosis quality care. We found that despite existing recommendations, half or more patients with cirrhosis had no HCC or EV surveillance, or test for PT/INR during the study follow up period.

Our results of a low overall rate of 8.78% for every 6-12 months HCC surveillance among patients with cirrhosis in the U.S. are in line with a recent meta-analysis,[16] in which the pooled surveillance rate of HCC from population-based studies was 9.8%. We also noted that the population-based sub-analysis from this meta-analysis included one large study with a very high reported surveillance rate of about 50% because this study defined HCC surveillance loosely as having at least one liver imaging within the 2 years prior to a diagnosis of HCC. Therefore, the pooled rate could be even lower.[25] Our study added to the literature with data based on consistent surveillance method (liver imaging every 6-12 months) and drawn from a large nationwide cohort of patients with cirrhosis in the U.S. with private health insurance, further highlighting the poor care gap for cirrhosis patients overall as many may have less favorable health insurance coverage and access to care.

The low frequency of health monitoring is likely a result from non-adherence to recommendations on both patients' and providers' ends. Prior studies have found particular challenges encountered by PCP in directing cirrhosis-related management decisions due to a variety of patient medical and psychosocial challenges.[26] Engagement of advanced practice providers e.g. GI/hepatologists can lead to improved quality of care and 30-day readmission as well as survival outcomes for patients with cirrhosis.[27] Technologies such as smartphone

applications for remote monitoring may be helpful, though only 30% actually used the app despite 70% agreed to download them,[28] which may be due in part to the older age of patients with cirrhosis.

On the other hand, an encouraging finding from our study was that for those who were diagnosed in the years 2013-2016, their adjusted odds of having testing and imagining were about 1.1 to 1.3 times greater than those diagnosed between 2007-2009. This increase may reflect the impact of updated guidelines and recommendations on the quality of care for those with cirrhosis which were originally published in 2010 and were most recently updated in 2019.[10, 14]

We recognize the following limitations. Our study only included data for privately insured people, so results may not be generalized to those with other types of insurance. However, given that those with private insurance are known to have better access to care, our observed metrics would be even lower among those without private insurance. Furthermore, patients in the study all had private insurance. The care gap in the U.S. found in this study may not be generalizable to other countries, especially those with universal healthcare system or even to patients without private insurance in the U.S. Data from population-based studies from other countries are needed. Some patients may have had non-continuous enrolment during the study period. However, to account for this possibility, we established our inclusion criteria to only include those who had private insurance coverage for at least 60 days during each six-month period as noted in our methods section. We also performed a sensitivity analysis to include only patients who had continuous enrolment and found that the results were similar suggesting that inclusion criteria were robust enough not to cause a significant change in outcomes. Additionally, given that the study period spanned from 2007 to 2016, this date may not represent the patients' first diagnosis date of cirrhosis. Therefore, we determined the frequency of procedures or testing

that should be continuously performed at regular intervals but not just once such as hepatitis A and B vaccines. Similarly, it should be emphasized that patients without a diagnosis code of varices does not necessarily mean that the patients do not have varices, as it is only known by doing endoscopy. Therefore, patients with varices might be misclassified as without varices if no EV surveillance was done. This would bias the results towards higher percentage of EV surveillance in the subgroup of patient without history of varices. However, we still observed a very low percentage of frequency in this group. In addition, current recommendation on EV surveillance interval of every 1-3 years were based on severity of the cirrhosis and the finding of the initial endoscopy. Our analysis was not able to adjust for all these factors due to lack of endoscopy report. Some patients might be on non-selective beta-blockers and hence EV surveillance is not required. With regard to HCC surveillance, we were unable to determine whether the imaging was done for that particular purpose and will lead to overestimation of compliance. Finally, we were unable to obtain some demographic factors that may affect the screening rate such as levels of education, ethnicity, and laboratory results.

Conclusion

Despite having private health insurance, adherence to practice recommendations for laboratory, imaging, and endoscopy monitoring for complications of cirrhosis in our nationwide cohort of patients with cirrhosis was dismally low, especially in older patients and those without specialist care. Further research is needed to not only better characterize the barriers to care and but also to identify intervention such as utilization of APPs and/or innovative technologies to include remote monitoring smartphone applications that may improve the current state of cirrhosis care.

Abbreviations: Abd US: abdominal ultrasound; CBC: complete blood count; CCI: Charlson's comorbidity index; CMP: comprehensive metabolic panel; CPT: Current Procedural

Terminology; CT: computed tomography; EGD: esophagogastroduodenoscopy; HCC, hepatocellular carcinoma; HMO: Health Maintenance Organization; ICD: International Classification of Diseases; INR: international normalized ratio; MRI: magnetic resonance imaging; OLT: orthotopic liver transplantation; PPO: Preferred Provider Organization; PT prothrombin time; U.S.: United States.

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Author names in bold designate shared co-first authorship

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Table 1: Demographic characteristics of patients with cirrhosis, categorized by compensated and decompensated cirrhosis

	Overall (N= 82427)		Decompensated cirrhosis (N=39147)		Compensated cirrhosis (N=43280)		P value
	N	%	N	%	N	%	
Sex							
Male	45161	54.79	22295	56.95	22866	52.83	<.0001
Female	37266	45.21	16852	43.05	20414	47.17	
Age							
18-40	9604	11.65	4458	11.39	5146	11.89	<.0001
41-55	28885	35.04	12933	33.04	15952	36.86	
>55	43938	53.31	21756	55.58	22182	51.25	
Insurance type							
HMO	9292	11.27	4237	10.82	5055	11.68	<.0001
PPO	48770	59.17	22483	57.43	26287	60.74	
Others	24365	29.56	12427	31.74	11938	27.58	
Specialty							
GI/ID	44910	54.48	22512	57.51	22398	51.75	<.0001
PCP*	28055	34.04	12632	32.27	15423	35.64	
Other	9462	11.48	4003	10.23	5459	12.61	
Year**							
2007-2009	23562	28.59	10324	26.37	13238	30.59	<.0001
2010-2012	30475	36.97	15319	39.13	15156	35.02	
2013-2016	28390	34.44	13504	34.50	14886	34.39	
Region							
North East	15950	19.35	7608	19.43	8342	19.27	<.0001
North Central	18700	22.69	9216	23.54	9484	21.91	
South	31091	37.72	14300	36.53	16791	38.80	
West	14768	17.92	7125	18.20	7643	17.66	
Etiology							

Viral hepatitis	1699	2.06	647	1.65	1052	2.43	<.0001
NAFLD	5669	6.88	2620	6.69	3049	7.04	
Alcohol-associated liver disease	2345	2.84	1561	3.99	784	1.81	
Others	72714	88.22	34319	87.67	38395	88.71	
CCI* **							
0	32487	39.41	19530	49.89	12957	29.94	<.0001
1 to 2	28539	34.62	8368	21.38	20171	46.61	
3 to 4	14070	17.07	6683	17.07	7387	17.07	
≥5	7331	8.89	4566	11.66	2765	6.39	

Abbreviation: HMO: health maintenance organization, PPO: preferred provider organization, GI: gastroenterology, ID: infectious disease, PCP: primary care physician

*PCP is defined by family medicine, internal medicine, OB/Gyn, hospitalist.

**Year is defined by the year of index date

***We did not include liver-related diseases in CCI to avoid adjusting overlapped variables on multivariable models

Table 2. Factors associated with HCC surveillance in patients with cirrhosis

	Univariable analysis			Multivariable analysis		
	Odds ratio	**95% CI**	**P value**	**Adjusted odds ratio**	**95% CI**	**P value**
Sex						
Male	1.00			1.00		
Female	0.93	(0.88 - 0.97)	0.0017	0.95	(0.93 - 1.02)	0.3045
Age						
18-40	1.00			1.00		
41-55	1.17	(1.08 - 1.28)	0.0002	1.13	(0.99 - 1.19)	0.0518
>55	1.08	(1.00 - 1.18)	0.0522	1.05	(0.93 - 1.10)	0.8161
Insurance type						
HMO	1.00			1.00		
PPO	1.20	(1.11 - 1.30)	<.0001	1.16	(1.06 - 1.25)	0.0010
Others	1.04	(0.95 - 1.13)	0.4369	0.99	(0.90 - 1.08)	0.8114
Specialty						
GI/ID	1.00			1.00		
PCP*	0.45	(0.43 - 0.48)	<.0001	0.48	(0.46 - 0.52)	<.0001
Other	0.72	(0.66 - 0.78)	<.0001	0.81	(0.75 - 0.88)	<.0001
Year**						
2007-2009	1.00			1.00		
2010-2012	0.86	(0.81 - 0.92)	<.0001	0.86	(0.81 - 0.92)	<.0001
2013-2016	1.32	(1.25 - 1.41)	<.0001	1.32	(1.28 - 1.45)	<.0001
Region						
North East	1.00			1.00		
North Central	1.13	(1.05 - 1.22)	0.0012	1.14	(1.06 - 1.24)	0.0005
South	1.13	(1.06 - 1.21)	0.0003	1.08	(1.01 - 1.16)	0.0310
West	0.93	(0.86 - 1.01)	0.0988	0.96	(0.87 - 1.03)	0.2299
Etiology						
Viral hepatitis	1.00			1.00		

NAFLD	1.51	(1.51 - 1.28)	<.0001	1.58	(1.33 - 1.88)	<.0001
Alcohol-associated liver disease	1.23	(1.23 - 1.01)	0.0381	1.09	(0.90 - 1.34)	0.3771
Others	0.72	(0.72 - 0.62)	<.0001	0.77	(0.66 - 0.91)	0.0014
Severity						
Compensated	1.00			1.00		
Decompensated	1.49	(1.42 - 1.57)	<.0001	1.51	(1.43 - 1.59)	<.0001
CCI* **						
0	0.90	(0.85 - 0.95)	0.0003	0.82	(0.77 - 0.88)	<.0001
1 to 2	1.00			1.00		
3 to 4	1.29	(1.20 - 1.38)	<.0001	1.15	(1.07 - 1.23)	0.0002
≥5	1.42	(1.31- 1.54)	<.0001	1.23	(1.13- 1.35)	<.0001

See table 1 for abbreviation and definition of *, **, and ***

Table 3. Factors associated with routine laboratory testing in patients with cirrhosis

	Univariable analysis			Multivariable analysis		
	Odds ratio	95% CI	P value	Adjusted odds ratio	95% CI	P value
Sex						
Male	1.00					
Female	0.98	(0.95 - 1.01)	0.1328			
Age						
18-40	1.00			1.00		
41-55	1.21	(1.15 - 1.27)	<.0001	1.16	(1.10 - 1.22)	<.0001
>55	0.97	(0.92 - 1.02)	0.2137	0.95	(0.90 - 1.00)	0.0484
Insurance type						
HMO	1.00			1.00		
PPO	1.06	(1.01 - 1.11)	0.0179	0.99	(0.4 - 1.04)	0.7425
Others	0.76	(0.72 - 0.80)	<.0001	0.74	(0.70 - 0.78)	<.0001
Specialty						
GI/ID	1.00			1.00		
PCP*	0.64	(0.62 - 0.66)	<.0001	0.68	(0.66 - 0.70)	<.0001
Other	0.87	(0.83 - 0.92)	<.0001	0.94	(0.90 - 0.99)	0.0210
Year**						
2007-2009	1.00			1.00		
2010-2012	0.85	(0.82 - 0.88)	<.0001	0.88	(0.85 - 0.92)	<.0001
2013-2016	1.20	(1.15 - 1.24)	<.0001	1.25	(1.20 - 1.30)	<.0001
Region						
North East	1.00			1.00		
North Central	1.34	(1.28 - 1.41)	<.0001	1.33	(1.27 - 1.40)	<.0001
South	1.50	(1.43 - 1.56)	<.0001	1.41	(1.35 - 1.48)	<.0001
West	1.08	(1.03 - 1.14)	0.0027	1.04	(0.98 - 1.10)	0.1944
Etiology						
Viral hepatitis	1.00			1.00		

NAFLD	1.39	(1.24 - 1.56)	<.0001	1.43	(1.27 - 1.61)	<.0001
Alcohol-associated liver disease	1.46	(1.28 - 1.67)	<.0001	1.38	(1.20 - 1.58)	<.0001
Others	0.90	(0.81 - 0.99)	0.0484	0.93	(0.83 - 1.03)	0.1713
Severity						
Compensated	1.00			1.00		
Decompensated	1.18	(1.14 - 1.21)	<.0001	1.17	(1.13 - 1.21)	<.0001
CCI* **						
0	0.99	(0.95 - 1.02)	0.4162	0.99	(0.95 - 1.03)	0.6366
1 to 2	1.00			1.00		
3 to 4	1.21	(1.16 - 1.26)	<.0001	1.17	(1.12 - 1.23)	<.0001
≥5	1.37	(1.30 - 1.45)	<.0001	1.37	(1.29 - 1.45)	<.0001

See table 1 for abbreviation and definition of *, **, and ***

Table 4. Factors associated with prothrombin and international normalized ratio testing in patients with cirrhosis

	Univariable analysis			Multivariable analysis		
	Odds ratio	95% CI	P value	Adjusted odds ratio	95% CI	P value
Sex						
Male	1.00			1.00		
Female	0.84	(0.80 - 0.88)	<.0001	0.90	(0.86 - 0.95)	<.0001
Age						
18-40	1.00			1.00		
41-55	1.41	(1.29 - 1.53)	<.0001	1.27	(1.17 - 1.39)	<.0001
>55	1.19	(1.10 - 1.30)	<.0001	1.11	(1.02 - 1.20)	0.0209
Insurance type						
HMO	1.00			1.00		
PPO	1.06	(0.98 - 1.14)	0.1455	1.00	(0.92 - 1.08)	0.9729
Others	0.80	(0.74 - 0.87)	<.0001	0.77	(0.70 - 0.84)	<.0001
Specialty						
GI/ID	1.00			1.00		
PCP*	0.49	(0.46 - 0.52)	<.0001	0.55	(0.51 - 0.58)	<.0001
Other	0.78	(0.73 - 0.84)	<.0001	0.85	(0.78 - 0.92)	<.0001
Year**						
2007-2009	1.00			1.00		
2010-2012	0.79	(0.75 - 0.84)	<.0001	0.80	(0.75 - 0.85)	<.0001
2013-2016	1.02	(0.96 - 1.08)	0.6198	1.07	(1.00 - 1.13)	0.0375
Region						
North East	1.00			1.00		
North Central	1.27	(1.18 - 1.37)	<.0001	1.26	(1.16 - 1.36)	<.0001
South	1.37	(1.28 - 1.47)	<.0001	1.30	(1.21 - 1.40)	<.0001
West	1.12	(1.03 - 1.21)	0.0094	1.08	(0.99 - 1.18)	0.0648
Etiology						

Viral hepatitis	1.00			1.00		
NAFLD	2.07	(1.74 - 2.47)	<.0001	2.00	(1.68 - 2.40)	<.0001
Alcohol-associated liver disease	2.29	(1.89 - 2.77)	<.0001	1.87	(1.54 - 2.27)	<.0001
Others	0.83	(0.70 - 0.97)	0.023	0.83	(0.70 - 0.98)	0.0253
Severity						
Compensated	1.00			1.00		
Decompensated	1.83	(1.75 - 1.93)	<.0001	1.77	(1.68 - 1.87)	<.0001
CCI* **						
0	1.16	(1.10 - 1.23)	<.0001	1.03	(0.97 - 1.09)	0.4076
1 to 2	1.00			1.00		
3 to 4	1.39	(1.29 - 1.49)	<.0001	1.21	(1.12 - 1.30)	<.0001
≥5	1.48	(1.36 - 1.61)	<.0001	1.26	(1.15 - 1.38)	<.0001

See table 1 for abbreviation and definition of *, **, and ***

Table 5. Factors associated with EV surveillance in patients with cirrhosis

	Univariable analysis			Multivariable analysis		
	Odds ratio	95% CI	P value	Adjusted odds ratio	95% CI	P value
Sex						
Male	1.00			1.00		
Female	0.89	(0.85 - 0.93)	<.0001	0.99	(0.95 - 1.04)	0.7516
Age						
18-40	1.00			1.00		
41-55	1.41	(1.30 - 1.53)	<.0001	1.09	(0.99 - 1.18)	0.0636
>55	1.35	(1.25 - 1.46)	<.0001	1.08	(0.99 - 1.17)	0.0890
Insurance type						
HMO	1.00			1.00		
PPO	1.22	(1.13 - 1.32)	<.0001	1.17	(1.08 - 1.26)	0.0002
Others	1.03	(0.95 - 1.12)	0.4791	1.01	(0.92 - 1.10)	0.8489
Specialty						
GI/ID	1.00			1.00		
PCP*	0.24	(0.23 - 0.26)	<.0001	0.32	(0.30 - 0.34)	<.0001
Other	0.58	(0.53 - 0.62)	<.0001	0.70	(0.65 - 0.76)	<.0001
Year**						
2007-2009	1.00			1.00		
2010-2012	0.93	(0.87 - 0.98)	0.0085	0.96	(0.90 - 1.02)	0.1429
2013-2016	1.29	(1.22 - 1.37)	<.0001	1.29	(1.22 - 1.37)	<.0001
Region						
North East	1.00			1.00		
North Central	1.27	(1.19 - 1.36)	<.0001	1.29	(1.20 - 1.39)	<.0001
South	1.18	(1.11 - 1.26)	<.0001	1.07	(1.00 - 1.15)	0.0471
West	1.12	(1.04 - 1.20)	0.0041	1.15	(1.06 - 1.25)	0.0005
Etiology						
Viral hepatitis	1.00			1.00		
NAFLD	1.61	(1.37 - 1.90)	<.0001	1.39	(1.16 - 1.65)	0.0003

Alcohol-associated liver disease	1.47	(1.22 - 1.77)	<.0001	1.11	(0.91 - 1.36)	0.2939
Others	0.83	(0.71 - 0.96)	0.0138	1.04	(0.88 - 1.22)	0.6588
Existence of varices						
Without varices	1.00			1.00		
With varices	5.90	(5.62 - 6.19)	<.0001	4.60	(4.36 - 4.84)	<.0001
CCI* **						
0	0.83	(0.79 - 0.88)	<.0001	0.76	(0.71 - 0.80)	<.0001
1 to 2	1.00			1.00		
3 to 4	1.61	(1.52 - 1.71)	<.0001	1.12	(1.05 - 1.20)	0.0007
≥5	1.59	(1.47 - 1.71)	<.0001	1.17	(1.08 - 1.27)	0.0002

See table 1 for abbreviation and definition of *, **, and **

Figure legend

Figure 1. The frequency of procedure/testing among patient with cirrhosis, categorized by overall, decompensated (DC) and compensated cirrhosis (CC). (A) HCC surveillance (B) CBC or CMP (C) PT/INR. X axis represents the proportion of patients with cirrhosis who underwent the testing/procedures, Y axis denotes the subgroup of different frequencies.

Figure 2. The frequency of esophageal varices surveillance among patient with cirrhosis, categorized by no varices, varices without bleeding, and varices with bleeding. EV: esophageal varices. X axis represents the proportion of patients with cirrhosis who underwent the testing/procedures, Y axis denotes the subgroup of different frequencies.

Figure 1. The frequency of procedure/testing among patient with cirrhosis, categorized by overall, decompensated (DC) and compensated cirrhosis (CC).

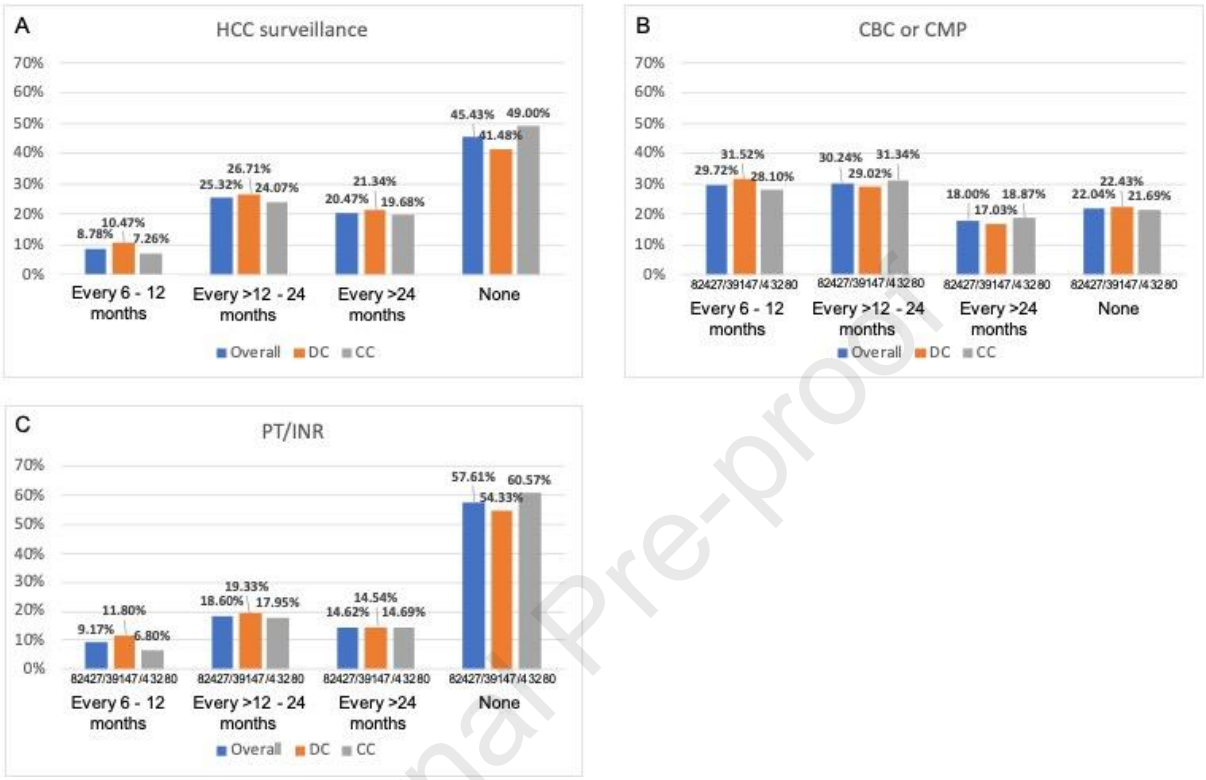
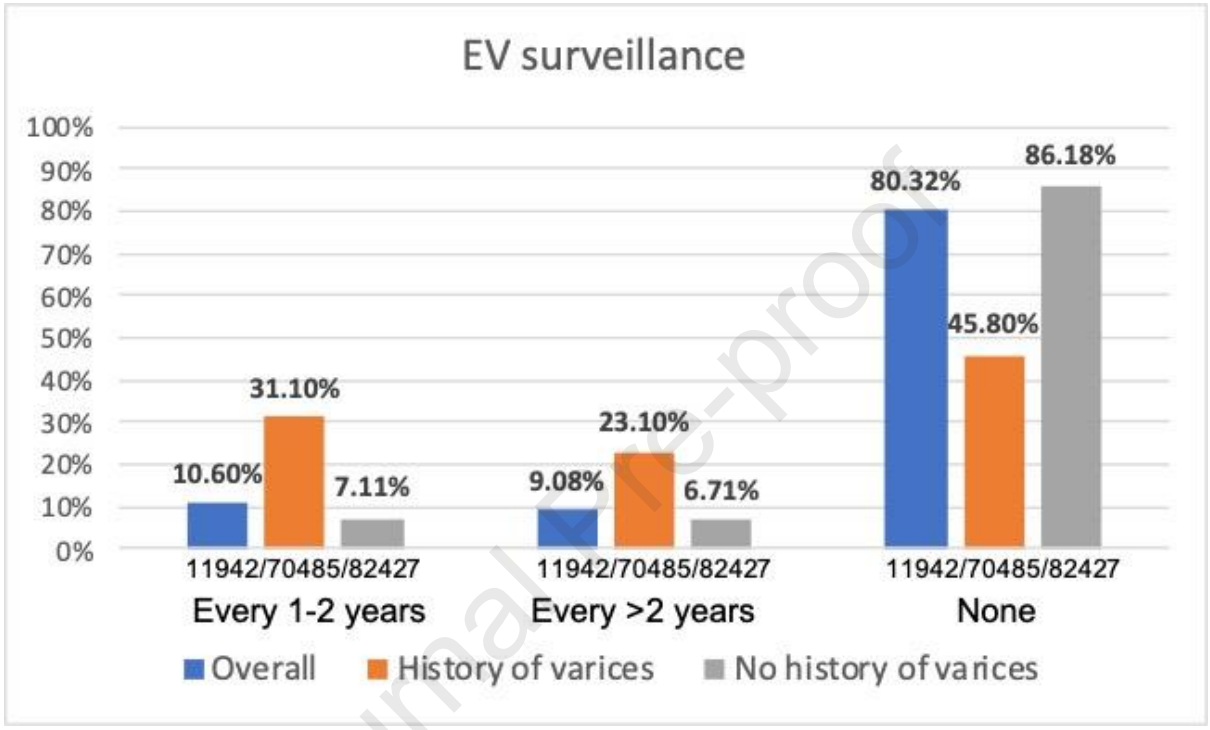


Figure 2. The frequency of esophageal varices surveillance among patient with cirrhosis, categorized by no varices, varices without bleeding, and varices with bleeding.



Highlights

- The adherence of monitoring/surveillance for liver complications was assessed by determining the frequency of procedure/laboratory test in patients with cirrhosis.
- We showed a disappointing adherent rate of HCC surveillance (8.78%), laboratory testing (29.72%) at least every 6-12 months, or EV surveillance (10.6%) at least every 1-2 years, although there was an improvement in recent years.
- Age, insurance plan, being followed up by specialist, severity of cirrhosis, and comorbidities played important role in predicting the adherence of health monitoring.