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Original Article

Impact of all-oral direct-acting antivirals on hepatocellular carcinoma in Vietnamese patients with chronic HCV genotype 1

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Abstract

Introduction: Hepatitis C virus (HCV) genotype 1 is a significant cause of hepatocellular carcinoma (HCC) in Vietnam. Direct-acting antivirals (DAAs) are effective in achieving sustained virologic response (SVR), potentially reducing HCC incidence. This study evaluated how DAA regimens affect HCC incidence in Vietnamese patients with chronic liver disease related to HCV genotype 1.

Methodology: A retrospective cohort study was conducted with 450 HCV-1 patients treated with DAAs at the Liver Clinic, University Medical Center Ho Chi Minh City, Vietnam. Patients were followed for a median duration of 0.5 years. Treatment regimens included combinations of NS5A inhibitors with NS3/4A protease inhibitors or NS5B polymerase inhibitors. Data on demographics, baseline clinical characteristics (e.g., alpha-fetoprotein, albumin levels), and liver function were collected before initiating DAA treatment. Follow-up data, including SVR rates and HCC incidence, were assessed at the end of treatment and during the post-treatment observation period (median follow-up of 0.5 years). This approach allowed us to compare pre-treatment baseline data with post-treatment outcomes to evaluate the impact of DAA therapy on HCC risk factors and incidence.

Results: SVR was achieved in 94.8% of patients, with an HCC incidence of 1.1% at 1 year for SVR patients, versus 6.5% for non-SVR patients. Significant risk factors for HCC included hypoalbuminemia, elevated alpha-fetoprotein levels, and non-SVR status.

Conclusions: DAAs significantly reduce HCC incidence in Vietnamese patients with HCV-1; however, ongoing surveillance is essential for high-risk patients.

Key words: DAA; HCC; cirrhosis; SVR; HCV genotype 1.

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Introduction

Hepatitis C virus (HCV) infection is a major global health concern, often leading to chronic hepatitis infection, cirrhosis, and hepatocellular carcinoma (HCC). Approximately 70% of individuals infected with HCV develop chronic HCV infection, significantly increasing the risk of severe liver conditions. According to the World Health Organization (WHO), around 50 million people globally live with chronic HCV infection, with substantial regional variations in prevalence [1]. Without treatment, a significant proportion of these individuals are at risk of progressing to cirrhosis or HCC [2–4].

Direct-acting antivirals (DAAs) have revolutionized HCV treatment, achieving high cure rates with shorter treatment durations and fewer side effects than interferon-based therapies [5]. The DAAs target specific steps in the HCV life cycle, effectively suppressing viral replication. These regimens typically involve combinations of drugs that inhibit viral proteins such as NS5A, NS5B polymerase, and NS3/4A protease. Studies have demonstrated that achieving a sustained virological response (SVR) with DAA therapy significantly reduces the risk of liver-related complications, including HCC [5].

Despite the proven efficacy of DAAs in eradicating HCV, the impact of these therapies on the development of HCC in patients with chronic liver disease remains an area of active research. Several studies suggest that while DAAs reduce the overall risk of HCC, certain factors such as advanced liver fibrosis, baseline alpha-fetoprotein levels, and patient demographics may influence the likelihood of developing HCC post-treatment [6,7].

Although numerous studies have evaluated the impact of direct-acting antiviral agents (DAAs) on HCC incidence, data on Vietnamese patients with HCV genotype 1 (HCV-1) remain limited. The specific epidemiological and genetic context in Southeast Asia,

especially in Vietnam, may influence disease progression and treatment response, underscoring the need for focused research on this population. This study aims to provide valuable insights on post-treatment risk factors, contributing to the refinement of monitoring strategies for high-risk patients in resource-limited settings.

Methodology

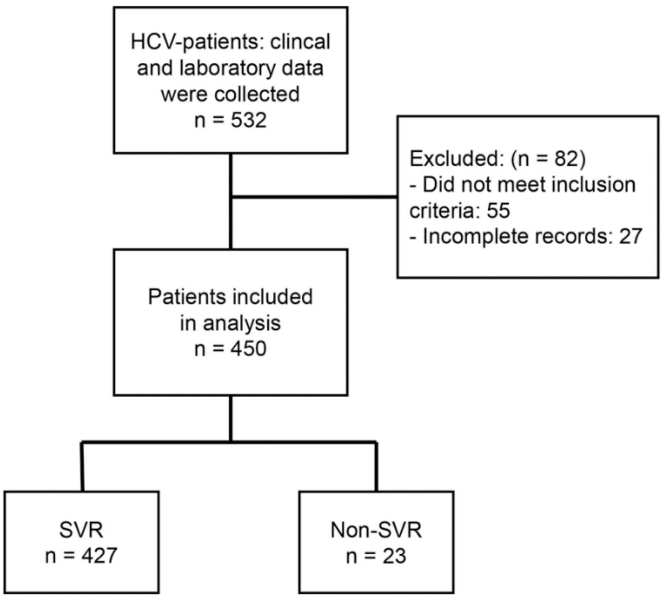
Study design

This is a retrospective cohort study designed to evaluate the impact of all-oral DAA regimens on the incidence of HCC in patients with chronic HCV-1 infection, with or without cirrhosis.

Study population

The study included patients diagnosed with chronic HCV-1 infection who were treated with DAA regimens at the Liver Clinic, University Medical Center Ho Chi Minh City, between November 2020 and April 2021. Cirrhosis was diagnosed based on a combination of clinical presentation, imaging findings (ultrasound or CT indicating liver surface nodularity or splenomegaly), and laboratory markers (such as platelet count < 150 x 10^9/L), in accordance with established hepatology guidelines. This approach ensured consistent identification of cirrhosis across all participants. The inclusion criteria were: adult patients (aged 18 years and older), confirmed diagnosis of HCV-1 infection, completion of an all-oral DAA regimen, and no history of HCC prior to and during DAA treatment. The inclusion criteria required all patients to undergo comprehensive HCC screening prior to initiating DAA therapy, including imaging (ultrasound or computed tomography (CT)) and biomarker (alpha-fetoprotein) assessments. Only patients without detectable HCC at baseline were included, ensuring that the study focused on the incidence of new or developing HCC cases post-treatment. Exclusion criteria included: coinfection with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), incomplete medical records, and failure to complete the prescribed DAA regimen.

Figure 1. Flowchart of participants' disposition throughout the study.



HCV: hepatitis C virus; SVR: sustained virological response.

Treatment regimens

The DAA regimens administered included combinations of: NS5A inhibitors (e.g., ledipasvir, velpatasvir, daclatasvir), NS5B polymerase inhibitors (e.g., sofosbuvir), and NS3/4A protease inhibitors (e.g., simeprevir, grazoprevir, paritaprevir). The treatment durations ranged from 12 to 24 weeks, based on the specific regimen and patient characteristics, such as the presence of liver cirrhosis or previous treatment history.

Data collection

Data on demographics, baseline clinical characteristics (e.g., alpha-fetoprotein, albumin levels), and liver function were collected before initiating DAA treatment. All patients had chronic liver disease due to HCV-1 infection, including both non-cirrhotic and cirrhotic cases. Follow-up data, including SVR rates and HCC incidence, were assessed at the end of treatment and during the post-treatment observation period (median follow-up of 0.5 years). This approach allowed us to compare pre-treatment baseline data with post-treatment outcomes to evaluate the impact of DAA therapy on HCC risk factors and incidence (Figure 1).

Outcome measures

The primary outcome measure was the incidence of HCC during the follow-up period. The HCC was diagnosed based on imaging findings (CT or magnetic resonance imaging (MRI)) consistent with liver lesions typical of HCC, with elevated alpha-fetoprotein levels, following established guidelines. Secondary outcome measures included the rates of SVR and identification of significant risk factors for HCC development post-treatment.

Follow-up and monitoring

Patients were followed up for a median duration of 0.5 years post-treatment. Monitoring was conducted

Table 1. Baseline characteristics of patients with HCV-1: non-cirrhotic vs. cirrhotic groups.

Variable	Non-cirrhotic group (n = 270)	Cirrhotic group (n = 180)	*p* value
Age, years (mean ± SD)	54.8 ± 11.3	57.0 ± 10.5	0.04
Male, n (%)	130 (48.1%)	90 (50.0%)	0.71
Albumin, g/dL (mean ± SD)	3.7 ± 0.5	3.2 ± 0.6	*< 0.001*
Alpha-fetoprotein, ng/mL (mean ± SD)	10.2 ± 4.3	16.1 ± 6.8	*< 0.001*
Platelet count (×10⁹/L)	170 ± 45	125 ± 42	*< 0.001*
SVR, n (%)	259 (95.9%)	168 (93.3%)	0.21
Non-SVR, n (%)	11 (4.1%)	12 (6.7%)	—

Statistically significant differences ($p < 0.05$). HCV-1: hepatitis C virus genotype 1.

every 3 months, including clinical evaluations and imaging studies (ultrasound, CT scans) to detect the development of HCC. Laboratory tests, such as liver function tests and alpha-fetoprotein levels, were performed at each follow-up visit.

Statistical analysis

Cumulative HCC rates were calculated at 1 and 2 years' post-treatment. Univariate and multivariate analyses were conducted to identify significant risk factors associated with HCC development. Factors evaluated included hypoalbuminemia, thrombocytopenia, high alpha-fetoprotein levels, and SVR status. Logistic regression was selected to assess risk factors for HCC due to the short follow-up duration, but future analyses will incorporate survival methods to account for censoring. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using SPSS software (version 25.0).

Ethical considerations

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and was approved by the Biomedical Research Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City (Approval No. 678/HDDD-DHYD). Written informed consent was obtained from all participants prior to data collection. Patient confidentiality was strictly maintained, and all data were anonymized for analysis.

Results

Patient characteristics

A total of 450 patients with chronic HCV genotype 1 infection were included in the study, of whom 40% were diagnosed with liver cirrhosis at baseline based on clinical, imaging, and laboratory criteria. Among them, 270 patients (60.0%) did not have cirrhosis at baseline, including 130 males and 140 females, while 180 patients (40.0%) had cirrhosis, with an equal gender distribution of 90 males and 90 females. Baseline characteristics were compared between SVR and non-SVR groups (Table 1). Patients with non-SVR had significantly higher baseline alpha-fetoprotein levels ($p = 0.02$) and lower albumin levels ($p = 0.01$). The mean age of the overall cohort was 55.7 ± 11.0 years. There were 220 males and 230 females. Among patients with cirrhosis (n = 180), 90 were male and 90 were female; in the non-cirrhotic group (n = 270), 130 were male and 140 were female. The mean age was 56.3 ± 10.9 years in males and 55.1 ± 11.2 years in females, with no statistically significant difference ($p = 0.18$). The baseline albumin level averaged 3.5 g/dL, and the mean platelet count was 153 × 10^9/L. The average baseline alpha-fetoprotein level was 12.8 ng/mL.

Treatment regimens and SVR rates

The patients were treated with various DAA regimens tailored to their clinical condition, including the presence or absence of cirrhosis. Treatment regimens consisted of sofosbuvir + ledipasvir (n = 110), sofosbuvir + velpatasvir (n = 140), sofosbuvir + daclatasvir (n = 100), and sofosbuvir + velpatasvir + voxilaprevir (n = 100). Among the sofosbuvir +

Table 2. Treatment regimens and SVR rates for HCV-1.

Regimen	Disease type	Male (n)	Female (n)	Total (n)	SVR rate (%)
Sofosbuvir + Ledipasvir	Non-cirrhotic	30	30	60	94.4
	Cirrhotic	25	25	50	92.0
Sofosbuvir + Velpatasvir	Non-cirrhotic	42	43	85	96.0
	Cirrhotic	27	28	55	94.5
Sofosbuvir + Daclatasvir	Non-cirrhotic	28	32	60	93.3
	Cirrhotic	20	20	40	94.0
Sofosbuvir + Velpatasvir + Voxilaprevir	Non-cirrhotic	33	32	65	96.9
	Cirrhotic	17	18	35	94.3

HCV-1: hepatitis C virus genotype 1; SVR: sustained virological response.

Table 3. Incidence of HCC in HCV-1 patients by cirrhosis status, gender, SVR status, and follow-up duration.

Group	Male (n)	Female (n)	SVR (n, %)	Non-SVR (n, %)	Followed ≥ 0.5 yr	Followed ≥ 1 yr	Followed ≥ 2 yr	HCC Cases (n)	1-Year HCC Rate (%)	2-Year HCC Rate (%)
Non-cirrhotic	130	140	259 (95.9%)	11 (4.1%)	270	165	60	3	0.5	0.9
Cirrhotic	90	90	168 (93.3%)	12 (6.7%)	180	115	35	9	2.8	3.4
Total	220	230	427 (94.8%)	23 (5.2%)	450	280	95	12	1.3	1.7

HCC: hepatocellular carcinoma; HCV-1: hepatitis C virus genotype 1.

ledipasvir group, 60 patients were non-cirrhotic (30 males, 30 females), and 50 were cirrhotic (25 males, 25 females). In the sofosbuvir + velpatasvir group, 85 were non-cirrhotic (42 males, 43 females), and 55 were cirrhotic (27 males, 28 females). In the sofosbuvir + daclatasvir group, 60 patients were non-cirrhotic (28 males, 32 females), and 40 were cirrhotic (20 males, 20 females). In the sofosbuvir + velpatasvir + voxilaprevir group, 65 were non-cirrhotic (33 males, 32 females), and 35 were cirrhotic (17 males, 18 females). There was no significant difference in regimen uptake across gender or disease status ($p > 0.05$). The overall SVR rate among HCV-1 patients was 94.8%, with individual regimen SVR rates ranging from 93.8% to 96.0%. Specifically, the sofosbuvir + ledipasvir regimen achieved an SVR rate of 94.4%, sofosbuvir + velpatasvir achieved 95.3%, sofosbuvir + daclatasvir achieved 93.8%, and the combination of sofosbuvir + velpatasvir + voxilaprevir achieved 96.0% (Table 2).

Incidence of hepatocellular carcinoma

During the follow-up period (median duration: 0.5 years), 12 patients developed HCC. Specifically, 450 patients were followed for at least 6 months, 280 patients for 1 year, and 95 patients for 2 years. Among those followed for ≥ 1 year, 140 were male and 140 were female; among those followed for ≥ 2 years, 50 were male and 45 were female. There was no statistically significant difference in follow-up duration by gender ($p > 0.05$). The cumulative HCC rates at 1 and 2 years were 1.3% and 1.7%, respectively. The rates were notably lower in patients who achieved SVR compared to those who did not, underscoring the protective effect of achieving virological cure.

The incidence of HCC was significantly higher in patients who did not achieve SVR (6.5% at 1 year and 8.7% at 2 years) compared to those who did achieve SVR (1.1% at 1 year and 1.5% at 2 years), with a p value < 0.05, indicating statistical significance (Table 3).

Risk factors for HCC development

Univariate and multivariate analyses identified several significant risk factors for HCC development. Hypoalbuminemia (albumin levels < 3.5 g/dL) was associated with a significantly increased risk of HCC, with an odds ratio (OR) of 2.65 (95% CI: 1.32–5.03, $p = 0.004$). Elevated baseline alpha-fetoprotein levels (≥ 20 ng/mL) also emerged as a strong predictor of HCC, with an OR of 3.15 (95% CI: 1.68–5.92, $p < 0.001$). Additionally, patients who did not achieve SVR were at the highest risk for HCC, with an OR of 4.45 (95% CI: 2.21–8.94, $p < 0.001$). Thrombocytopenia (platelet count < 150 x 10^9/L) was also evaluated, but did not reach statistical significance in the multivariate analysis (OR: 1.85, 95% CI: 0.94–3.63, $p = 0.064$) (Table 4).

Additional subgroup analyses were conducted to explore the impact of baseline cirrhosis on HCC incidence and treatment outcomes. Among the 180 patients with cirrhosis at baseline, the SVR rate was slightly lower at 92.8% compared to 96.0% in non-cirrhotic patients. The incidence of HCC was also higher in the cirrhotic group, with cumulative rates of 2.8% at 1 year and 3.4% at 2 years, compared to 0.5% at 1 year and 0.9% at 2 years in non-cirrhotic patients (Table 3). Among the total cohort, 280 patients (140 males and 140 females) were followed for at least 1 year, including 115 cirrhotic and 165 non-cirrhotic patients. A total of 95 patients (50 males and 45 females) were followed for 2 years, comprising 35 cirrhotic and 60 non-cirrhotic patients. The differences

Table 4. Risk factors for HCC development in HCV-1 patients, stratified by gender.

Risk factor	Univariate analysis (p value)	Multivariate OR (95% CI)	Multivariate p value	Male HCC Cases (n)	Female HCC Cases (n)	Gender effect (p value)
Hypoalbuminemia (< 3.5 g/dL)	0.003	2.65 (1.32–5.03)	0.004	7	4	0.09
Thrombocytopenia (< 150 ×10^9/L)	0.045	1.85 (0.94–3.63)	0.064	6	3	0.15
Elevated alpha-fetoprotein (≥ 20 ng/mL)	< 0.001	3.15 (1.68–5.92)	< 0.001	8	3	0.05
Non-SVR status	< 0.001	4.45 (2.21–8.94)	< 0.001	5	1	0.03

HCC: hepatocellular carcinoma; HCV-1: hepatitis C virus genotype 1.

in follow-up duration were primarily due to the staggered timing of patient enrollment. No statistically significant association was observed between follow-up duration and gender or disease group ($p > 0.05$). These findings highlight the continued risk of HCC in patients with advanced liver disease, even after achieving SVR.

Survival analysis of HCC incidence

Kaplan-Meier survival curves were generated to assess the cumulative incidence of HCC among patients with and without SVR during the follow-up period. The cumulative 1-year incidence of HCC was significantly lower in patients achieving SVR (1.1%) compared to those who did not (6.5%) (log-rank test, $p < 0.001$).

Cox proportional hazards regression further confirmed that non-SVR status was associated with a significantly increased risk of HCC (hazard ratio: 4.45, 95% CI: 2.21–8.94, $p < 0.001$). These findings align with the logistic regression analysis and underscore the protective effect of achieving SVR.

The Kaplan–Meier plots demonstrate early separation of the HCC risk curves, highlighting a rapid reduction in risk following the achievement of SVR. Patients were stratified into two groups: those with chronic hepatitis C without cirrhosis and those with chronic hepatitis C and baseline cirrhosis. Patients with cirrhosis exhibited significantly higher cumulative HCC rates compared to non-cirrhotic patients (log-rank test, $p = 0.02$), indicating an elevated residual risk despite viral clearance.

Discussion

The results of this study underscore the significant impact of all-oral DAA regimens on reducing the incidence of HCC in Vietnamese patients with chronic HCV-1 infection. The observed SVR rate of 94.8% among the 450 treated patients underscores the high efficacy of these DAA regimens in achieving viral eradication and substantially lowering the risk of serious liver-related complications, including hepatocellular carcinoma. However, the persistence of HCC development in a subset of patients despite achieving SVR points to the complex nature of liver disease management even after virological cure. While cirrhosis is a recognized risk factor for HCC and was prevalent in 40% of our study population, it was not included as a covariate in the multivariate analysis. This decision was based on the study's focus on evaluating post-treatment risk factors that may be directly influenced by DAA therapy, such as hypoalbuminemia and elevated alpha-fetoprotein levels. Since cirrhosis is already well-established as a predictor of HCC, the aim in this study was to identify additional modifiable factors that might stratify risk among patients achieving SVR. Nonetheless, we acknowledge the importance of cirrhosis as a baseline risk factor for HCC and suggest that future studies with larger cohorts and longer follow-up durations may further explore the interplay between cirrhosis and post-treatment risk factors for a more comprehensive risk assessment.

Efficacy of DAA regimens

The high SVR rates observed in this study align with those reported in other large-scale trials and real-world studies, demonstrating the effectiveness of DAA combinations such as sofosbuvir + ledipasvir, sofosbuvir + velpatasvir, sofosbuvir + daclatasvir, and sofosbuvir + velpatasvir + voxilaprevir [2,4]. These SVR rates, ranging from 93.8% to 96.0%, reaffirm the robustness of these treatments in managing HCV-1. Achieving SVR is crucial as it is associated with a significant reduction in the risk of liver-related morbidity and mortality, thereby enhancing the overall prognosis of patients.

Incidence and risk of HCC

Despite the overall success in achieving high SVR rates, the study found that 12 patients developed HCC during the follow-up period, with cumulative HCC rates of 1.3% at 1 year and 1.7% at 2 years. These rates are significantly lower compared to the pre-DAA era, reflecting the impact of effective antiviral therapy on reducing HCC risk. However, patients who did not achieve SVR had markedly higher HCC rates (6.5% at 1 year and 8.7% at 2 years), underscoring the importance of achieving virological cure to mitigate HCC risk [5].

The increased HCC risk in non-SVR patients may be attributed to ongoing liver inflammation and fibrosis progression, which continue to drive carcinogenesis despite partial viral suppression. This finding emphasizes the necessity for comprehensive and effective antiviral treatment strategies aimed at achieving SVR in all patients to reduce the long-term risk of HCC.

Identified risk factors for HCC

The study identified several significant risk factors for HCC development through univariate and multivariate analyses, highlighting the need for targeted post-treatment surveillance and intervention. The key risk factors included hypoalbuminemia, elevated baseline alpha-fetoprotein levels, and non-SVR status:

Hypoalbuminemia: Low albumin levels (< 3.5

g/dL) were significantly associated with an increased risk of HCC (odds ratio: 2.65, 95% CI: 1.32–5.03, p = 0.004). This finding aligns with other studies that have highlighted hypoalbuminemia as an indicator of advanced liver disease and poor prognosis [6]. Hypoalbuminemia may reflect decreased synthetic liver function and ongoing hepatic inflammation, both of which contribute to carcinogenesis. This underscores the importance of addressing and monitoring albumin levels as part of the comprehensive management of chronic HCV patients.

Elevated alpha-fetoprotein levels: Elevated alpha-fetoprotein levels (≥ 20 ng/mL) were a strong predictor of HCC (odds ratio: 3.15, 95% CI: 1.68–5.92, p < 0.001). Alpha-fetoprotein is a well-known biomarker for HCC, and elevated levels may indicate underlying malignancy or a predisposition to tumor development [7,8]. This highlights the necessity of regular monitoring of alpha-fetoprotein levels in patients with chronic HCV, even after achieving SVR. Continuous surveillance of this biomarker can aid in the early detection of HCC, facilitating timely intervention and improving patient outcomes.

Non-SVR status: Failure to achieve SVR was the most significant risk factor for HCC (odds ratio: 4.45, 95% CI: 2.21–8.94, p < 0.001). This highlights the protective effect of achieving viral eradication against the development of HCC, emphasizing the necessity of effective antiviral treatment [9]. Patients who do not achieve SVR should be closely monitored and considered for retreatment with alternative DAA regimens to reduce their HCC risk. Ensuring SVR not only mitigates the risk of liver disease progression but also significantly decreases the likelihood of HCC development.

It is also important to consider that some cases of HCC detected within the first year post-treatment may have been pre-existing but undetectable at baseline. Despite thorough baseline screening with imaging and alpha-fetoprotein assessments, small or early-stage HCC lesions may escape detection, particularly in patients with advanced liver disease. This reinforces the need for continued monitoring even in patients with initially negative screenings, as residual risk persists.

These findings underscore the critical importance of achieving SVR in HCV treatment, along with continuous monitoring of liver function and biomarkers in high-risk patients. Tailored surveillance and intervention strategies are essential for improving long-term outcomes and reducing the burden of HCC in patients with chronic HCV.

The findings of this study highlight several critical clinical implications. Achieving SVR should be a primary objective in managing HCV-1 to reduce the risk of HCC. This underscores the importance of adhering to treatment protocols and considering retreatment for non-responders [10]. The high efficacy of current DAA regimens supports their widespread use and efforts to ensure access for all eligible patients. Even after achieving SVR, patients with hypoalbuminemia, elevated alpha-fetoprotein levels, or cirrhosis require rigorous post-treatment surveillance for HCC. Regular imaging studies and alpha-fetoprotein testing are crucial for early detection and intervention [11]. Surveillance strategies should be tailored to individual risk profiles, with high-risk patients receiving more intensive monitoring. Identifying patients at higher risk for HCC enables targeted surveillance and early intervention strategies. This stratified approach can improve patient outcomes by facilitating timely detection and treatment of HCC, potentially enhancing survival rates [12]. Developing and validating risk stratification tools that incorporate clinical, biochemical, and genetic factors can improve the precision of HCC risk assessment in this population.

Our findings align with existing literature on the efficacy of DAAs in reducing HCC risk; however, they also add unique insights specific to the Vietnamese HCV-1 population. In contrast to broader studies, our analysis identifies hypoalbuminemia, elevated alpha-fetoprotein levels, and non-achievement of SVR as significant risk factors that require targeted post-treatment surveillance. This study highlights the importance of individualized monitoring approaches for high-risk groups, particularly in Southeast Asia, where hepatitis C prevalence and healthcare resources differ markedly from other regions. These findings could inform tailored surveillance strategies, optimizing long-term outcomes for patients in diverse epidemiological contexts.

While this study identifies key factors associated with post-SVR HCC risk, including hypoalbuminemia, elevated alpha-fetoprotein levels, and SVR status, we acknowledge the potential value of developing a comprehensive predictive model. Such a model could incorporate additional variables, including age, male gender, and composite indices such as aMAP and Fib-4, which have been associated with post-SVR HCC risk in prior studies. Future research could focus on integrating these variables into a predictive framework to improve risk stratification for post-SVR patients. A predictive model tailored to this population would offer clinicians a practical tool to guide surveillance intensity and prioritize interventions for high-risk patients.

Limitations

While the study provides valuable insights, it also has several limitations. The smaller sample size and shorter median follow-up period of 0.5 years compared to other studies may limit the comprehensiveness of the findings. Although the study offers important early post-treatment outcomes, future research with larger cohorts and longer follow-up periods is needed to better capture the long-term risk of HCC development after DAA therapy [13]. Additionally, while patients with detectable HCC were excluded at baseline based on imaging and biomarker (alpha-fetoprotein) assessments, it remains possible that some HCC cases detected within the first year post-treatment existed pre-treatment but were below the detection threshold. This limitation highlights the ongoing challenges of early HCC detection and the importance of post-treatment monitoring [14]. Finally, as a single-center study, the findings may not be generalizable to other populations or healthcare settings. Multi-center studies with diverse patient populations are needed to validate these results and enhance their applicability [15]. Longitudinal studies with extended follow-up periods are needed to better understand the long-term risk of HCC in patients treated with DAAs. These studies can provide more comprehensive data on the durability of SVR and the ongoing risk of liver complications [16]. Long-term follow-up will also help elucidate the potential late emergence of HCC in patients who achieve SVR by investigating the underlying mechanisms that link hypoalbuminemia and elevated alpha-fetoprotein levels to HCC development in the context of DAA treatment. Understanding these pathways can help develop targeted interventions to further reduce HCC risk [17]. Mechanistic studies may uncover novel biomarkers and therapeutic targets, enhancing the management of HCV-related liver disease. Developing and validating risk prediction models that integrate clinical, biochemical, and genetic factors to more accurately stratify patients' HCC risk post-SVR. This can lead to more personalized and effective surveillance protocols [18]. Advances in predictive modeling and precision medicine hold promise for optimizing post-treatment care and improving patient outcomes.

Conclusions

The study demonstrates the efficacy of all-oral DAA regimens in achieving high SVR rates and reducing HCC incidence in Vietnamese patients with HCV-1 related chronic liver disease. However, the persistent risk of HCC in certain subgroups highlights the need for continued vigilance and targeted post-treatment surveillance. By identifying key risk factors such as hypoalbuminemia, elevated alpha-fetoprotein levels, and non-SVR status, healthcare providers can better tailor follow-up strategies to improve patient outcomes and reduce the burden of HCC in this population. The integration of these findings into clinical practice can enhance the management of HCV and its complications, ultimately leading to better long-term health outcomes for patients with chronic HCV infection.

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Conflict of interests

No conflict of interests is declared.

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