Temporal change in etiology and clinical characteristics of hepatocellular carcinoma in New South Wales, Australia

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Introduction

Viral hepatitis and alcohol-related liver disease are the main risk factors for hepatocellular carcinoma (HCC) in many countries, including Australia. In Australia, given the access to HCV direct-acting antiviral (DAA) therapy since 2016, a temporal change in HCC etiology was hypothesized.

Aims

This study evaluated the temporal change in the etiology and characteristics of HCC in a large cohort of patients with HCC in New South Wales (NSW).

Methods

This was a retrospective cohort study of patients diagnosed with incident HCC between January 2008 and December 2021 and managed in three large public hospitals in NSW, Australia, including St Vincent's, Liverpool, and Westmead hospitals.

Patients were classified based on their HCC etiologies, ascertained from records in the clinical notes and laboratory results. Patients were classified as HCV-related HCC (HCV HCC) if they had a record of HCV diagnosis, confirmed by a positive HCV RNA, or had previously received HCV therapy. Patients were classified as HBV-related HCC (HBV HCC) if they had been diagnosed with a positive HBV surface antigen or had previously received HBV therapy. Etiologies including alcohol-related liver disease (ARLD), non-alcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) were identified based on multidisciplinary team reports. Other etiologies like autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, haemochromatosis, alpha-1-antitrypsin deficiency, or other liver diseases, were categorized as 'Others'. Patients with no documented underlying liver diseases were categorized as 'Nil/Unknown'.

Distribution of demographic and clinical characteristics was evaluated by HCC etiology and year of HCC diagnosis. Given that HCV DAA treatment has been government-funded and broadly available since March 2016 in Australia, an interrupted time series regression model was used to evaluate changes in the trend of the proportion of HCV HCC in each year during 2008-16 compared with 2017-21. Generalized linear models were used to evaluate the trend of the annual distribution of demographic and clinical characteristics of participants, assuming a binomial distribution of the dependent variables and a logit transformation as the link function.

Results

Of 1,394 patients who were diagnosed with HCC and managed in the three hospitals (2008-21), 1,370 patients were included in the analysis. Reasons for exclusion included insufficient medical records (n=3), combined HCC-cholangiocarcinoma (n=16) and fibrolamellar-HCC (n=5).

Table 1: Baseline characteristics of patients with HCC, overall and by HCC etiology

	Total (n=1370)	HCC etiology					
		HCV (n=483)	HBV (n=301)	ARLD (n=452)	NAFLD/NASH (n=347)	Others (n=64)	Nil/Unknown (n=58)
Age, years median (IQR)	65 (57-73)	60 (55-67)	61 (53-69)	63 (56-68)	71 (65-77)	73 (65-78)	75 (62-85)
Male gender, n (%)	1084 (79)	390 (81)	254 (84)	417 (92)	239 (69)	45 (70)	36 (62)
Born in Australia, n (%)	526 (38)	256 (53)	24 (8)	248 (55)	103 (30)	40 (63)	26 (45)
Aboriginal/Torres Strait Islander, n (%)	33 (2)	24 (5)	3 (1)	19 (4)	3 (1)	0 (0)	1 (2)
Co-morbidity as HCC etiology, n (%)*							
HCV	483 (35)	NA	19 (6)	187 (41)	21 (6)	2 (3)	NA
HBV	301 (22)	19 (4)	NA	34 (8)	19 (5)	3 (5)	NA
ARLD	452 (33)	187 (39)	34 (11)	NA	49 (14)	3 (5)	NA
NAFLD/NASH	347 (25)	21 (4)	19 (6)	49 (11)	NA	7 (11)	NA
Others	64 (5)	2 (<1)	3 (1)	3 (1)	7 (2)	NA	NA
Child-Pugh B/C, n (%)	408 (30)	147 (30)	72 (24)	195 (43)	89 (26)	16 (25)	8 (14)
MELD score >11, n (%)	458 (33)	156 (32)	87 (29)	205 (45)	124 (36)	18 (28)	7 (12)
Prior decompensation, n (%)	362 (26)	138 (29)	54 (18)	176 (39)	77 (22)	10 (16)	3 (5)
HCC detection via surveillance, n (%)	496 (36)	241 (50)	129 (43)	145 (32)	114 (33)	14 (22)	2 (3)
BCLC tumor stage O/A, n (%)	635 (46)	239 (49)	144 (48)	185 (41)	174 (50)	37 (58)	22 (38)
Single lesion < 3cm, n (%)	320 (23)	139 (29)	74 (25)	114 (25)	74 (21)	13 (20)	2 (3)
Curative HCC management, n (%)	466 (34)	162 (34)	123 (41)	118 (26)	127 (37)	26 (41)	16 (28)

* Percentages are not mutually exclusive in this analysis given that more than one etiology may be assigned to each patient

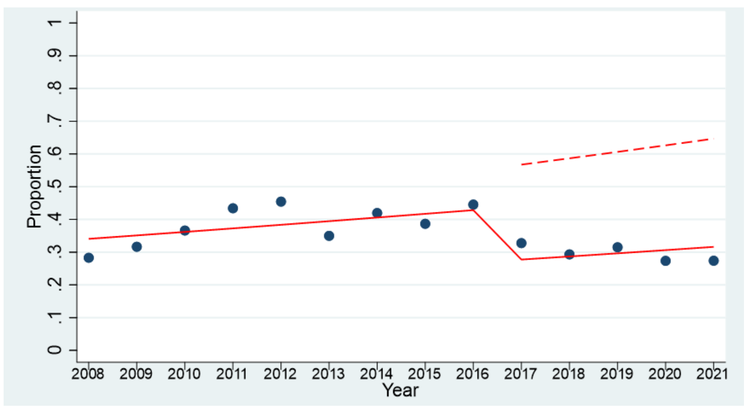

Figure 1: Annual proportion of patients with HCV-related HCC. Solid line: Actual trend over time. Dashed line: Predicted trend, assuming the pre-2016 trend continued. The trend changed significantly after 2016 (OR: 0.53; 95% CI 0.35–0.79; p=0.002)

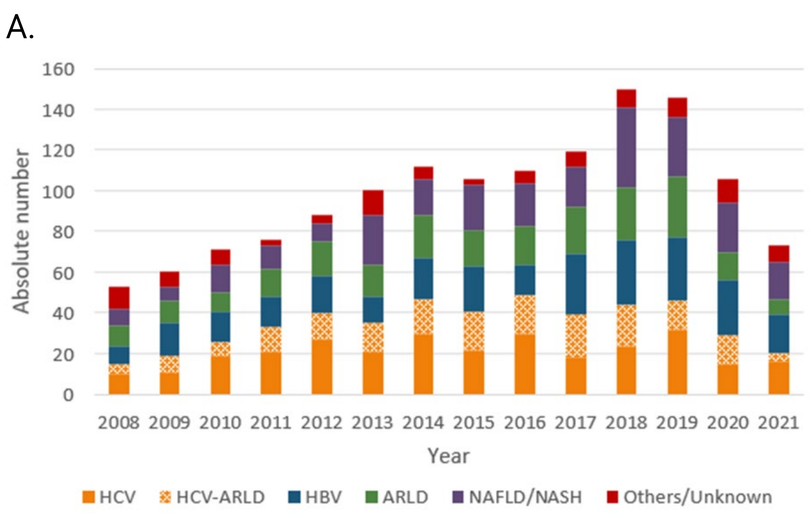

Figure 1: Annual absolute number (A) and proportion (B) of patients with HCC (2008-21), by HCC etiology. (ARLD: alcohol-related liver disease, NAFLD: non-alcoholic fatty liver disease, NASH: non-alcoholic steatohepatitis)

Linear trend for proportion of each HCC etiology (OR per annum):

- NAFLD/NASH: 1.05; 95% CI 0.97–1.14; p=0.200
- HBV: 0.95; 95% CI 0.88–1.02; p=0.166
- ARLD: 1.04; 95% CI 0.98–1.11; p=0.194

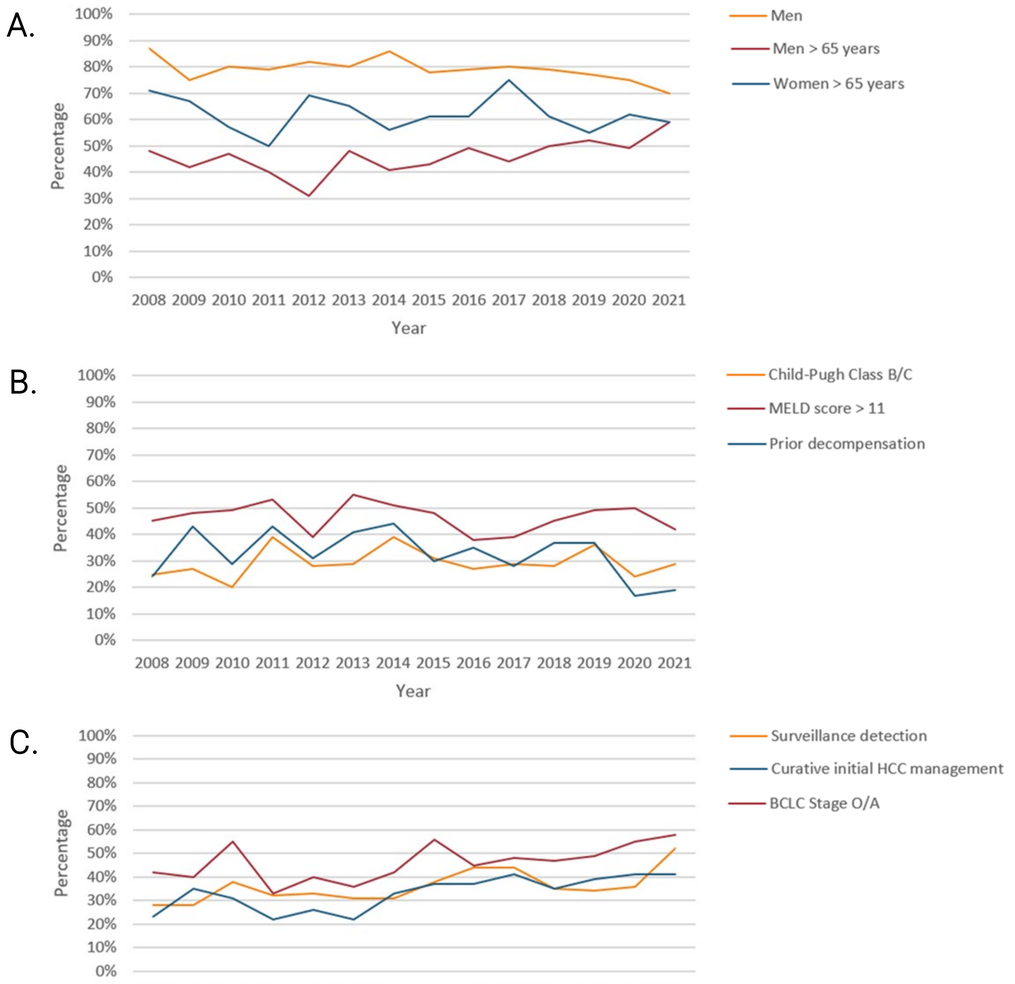

Figure 3: Annual proportion of patients with HCC (2008-21), by gender/age (A), underlying liver disease severity (B), and HCC clinical characteristics (C). MELD: model for end-stage liver; BCLC: Barcelona clinic liver cancer disease

Linear trend for proportion of each characteristics (OR per annum):

- Men: 0.97; 95% CI 0.93–1.00; p=0.068
- Men older than 65 years: 1.04; 95% CI 1.01–1.08; p=0.016
- Women older than 65 years: 0.99; 95% CI 0.93–1.06; p=0.760
- Prior decompensation: 0.96; 95% CI: 0.93–0.99; p=0.027
- Child-Pugh class B/C: 1.00; 95% CI: 0.97–1.04; p=0.793
- MELD score>11: 0.99; 95% CI: 0.96–1.02; p=0.457
- HCC detected through surveillance: 1.02; 95% CI: 0.99–1.05; p=0.186
- BCLC stage O/A: 1.05; 95% CI: 1.02–1.08; p=0.002
- Initial HCC curative management: 1.06; 95% CI: 1.03– 1.10; p<0.001

Conclusion

- This study demonstrated a decrease in the number of HCC cases after 2019, probably due to COVID-19-related restrictions.
- The number and proportion of patients with HCV HCC have been decreasing since DAA therapy became widely available, demonstrating the role of HCV elimination in decreasing HCC risk at population-level.
- The proportion of patients presenting with early-stage tumors has been increasing.
- Current healthcare policies should continue to promote HCV treatment and HCC surveillance following HCV cure among eligible patients. Moreover, other strategies should be developed for the prevention and management of emerging HCC risk factors including NAFLD/NASH.

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