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Validation and Comparison of Non-Invasive Tests for the Exclusion of High-Risk Varices in Compensated Advanced Chronic Liver Disease

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Abstract: Non-invasive tests (NITs) are a potential alternative to screening oesophagogastroduodenoscopy (OGD) for ruling out high-risk varices (HRVs) in patients with compensated advanced chronic liver disease (cACLD). This retrospective study aimed to externally validate and compare various NITs in a multi-centre Australian cohort. Patients with cACLD were enrolled between January 2013 and December 2022. Liver stiffness measurements (LSMs), clinicopathological data, and OGD results were collected. A total of 210 patients were included. The median age was 57 years and 65.7% were male. The main aetiology of cACLD was hepatitis C (41.9%), and 91.9% of patients were Child–Pugh A. HRV prevalence was 12.4%. The Baveno VI criteria (B6C) was the only NIT that could safely reduce the need for OGDs across all aetiologies of cACLD, with a negative predictive value of 98.6 and spared OGD in 33.8%. The FIB-4 would have avoided the most OGDs (71%); however, the HRV miss rate was 6%. The results suggest that the B6C is the best performing NIT in our cohort and reliably excludes HRVs in cACLD patients, regardless of aetiology. This study confirms that the Baveno VI criteria can be applied in an Australian, mixed aetiology cohort to avoid unnecessary screening OGD.

Keywords: Baveno VI; variceal bleeding; cirrhosis; oesophagogastroduodenoscopy

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1. Introduction

Compensated advanced chronic liver disease (cACLD) is a term introduced by the Baveno VI consensus to better reflect the spectrum of chronic liver disease and included patients with advanced chronic liver disease who were asymptomatic and had either severe fibrosis or compensated liver cirrhosis. This population of patients are at risk of developing clinically significant portal hypertension (CSPH) [1]. CSPH is defined as a hepatic venous pressure gradient (HVPG) $\geq$ 10 mmHg. It represents a critical milestone in the natural history of advanced chronic liver disease and has high clinical importance as it is associated with the development of various complications.

Oesophageal varices are a common manifestation of CSPH occurring in approximately 50% of patients with liver cirrhosis [2,3]. Acute variceal bleeding is the most serious decompensation event that directly affects patient survival and has a 6-week mortality rate of 15–20% [4]. Left untreated, recurrent haemorrhage is common and impacts 60% of patients, typically within 1–2 years of the initial bleed [5]. Progression of oesophageal varices size in patients with cirrhosis is associated with an increased risk of variceal bleeding [6]. A large prospective study has demonstrated that the size of small varices progressed at a rate of

12% in the first year, and 31% by the third year [7]. Varices with the highest risk of bleeding are large (>5 mm), have "red wale marks", and require prophylactic therapy to reduce the risk of bleeding either with the commencement of non-selective beta-blockers (NSBB) or endoscopic variceal ligation [3].

Oesophagogastroduodenoscopy (OGD) is accepted as the gold standard but is expensive, time consuming and an invasive method to detect oesophageal varices [3,8]. Due to the significant mortality associated with variceal bleeding, consensus guidelines recommend endoscopic screening for oesophageal varices in patients with a new diagnosis of cirrhosis [3,9]. However, endoscopic services may not be available or affordable in resource-limited localities. In addition to that, variceal screening has been significantly affected by the COVID-19 pandemic and subsequent backlogs, comprising almost a quarter of the delayed OGDs [10]. It is therefore essential that appropriate patients are captured to maximise the efficacy of the service and alleviate pressures on endoscopy waiting lists.

Although there are several well-validated scores for risk stratification and risk prediction in patients with decompensated liver cirrhosis, these are of limited use in the case of compensated cirrhosis. This has fostered interest in the development and use of non-invasive tools (NITs) for the assessment of patients with compensated cirrhosis and for the creation of screening tools for the diagnosis of high-risk varices (HRVs). Examples of NITs include the Baveno VI criteria (B6C), expanded Baveno VI criteria (E6BC), AST-to-platelet ratio index (APRI), Fibrosis 4 index (FIB-4), and the EVendo score [11–15]. The FIPS score, which was originally developed to predict post-transjugular intrahepatic portosystemic shunt (TIPS) survival, incorporates age, creatinine, albumin, and age, all of which are parameters associated with prognosis in advanced liver disease [16].

The B6C was recommended in the 2015 Baveno VI consensus workshop as a non-invasive alternative for HRV screening in patients with cACLD [11]. The criteria uses biochemical and non-invasive measurements to predict the presence of HRVs in patients with cACLD [11]. Based on the criteria, it is suggested that patients with a liver stiffness measurement (LSM) of <20 kPa and platelet count (PLT) > 150 $\times$ 10^9/L could safely avoid an OGD for variceal surveillance as the risk of developing HRVs is considered acceptably low (risk < 5%).

A recent meta-analysis of thirty studies by Stafylidou et al. demonstrated that the B6C is the most extensively validated and widely accepted NIT as a HRV screening tool [17]. However, there is currently no data of NIT performance in an Australian population. Hence, we aimed to externally validate and compare the B6C among other NITs which are commonly utilised as predictors of survival in patients with chronic liver disease [18,19]. We additionally sought to determine the sensitivity (SS), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV) of these NITs for the detection of HRVs.

2. Methods

Our multi-centre retrospective study involved the analysis of 13,029 transient elastographies over a 10-year period (1 January 2013–31 December 2022). Patients $\geq$18 years of age with cACLD were seen in the Department of Gastroenterology and Hepatology at Blacktown-Mount Druitt and Westmead Hospitals in the Western Sydney Local Health District. Diagnosis of cACLD was defined as asymptomatic patients with chronic liver disease and a LSM by transient elastography (TE) of $\geq$10 kPa. This was in accordance with the definition agreed upon in the Baveno VI workshop [11]. Those who had undergone OGD within 12 months and laboratory tests within 6 months of TE were included. Patients with a prior history of hepatic decompensation defined by the occurrence of jaundice, hepatic encephalopathy, ascites, or variceal bleeding were excluded. Patients were also excluded if they had prior oesophageal varices, portal vein thrombosis, non-cirrhotic portal hypertension, hepatocellular carcinoma (HCC), or were on non-selective beta-blocker (NSBB) therapy (Figure 1). The study was approved by the Western Sydney Local Health District Human Research Ethics Committee (Reference number: 2021/ETH00149).

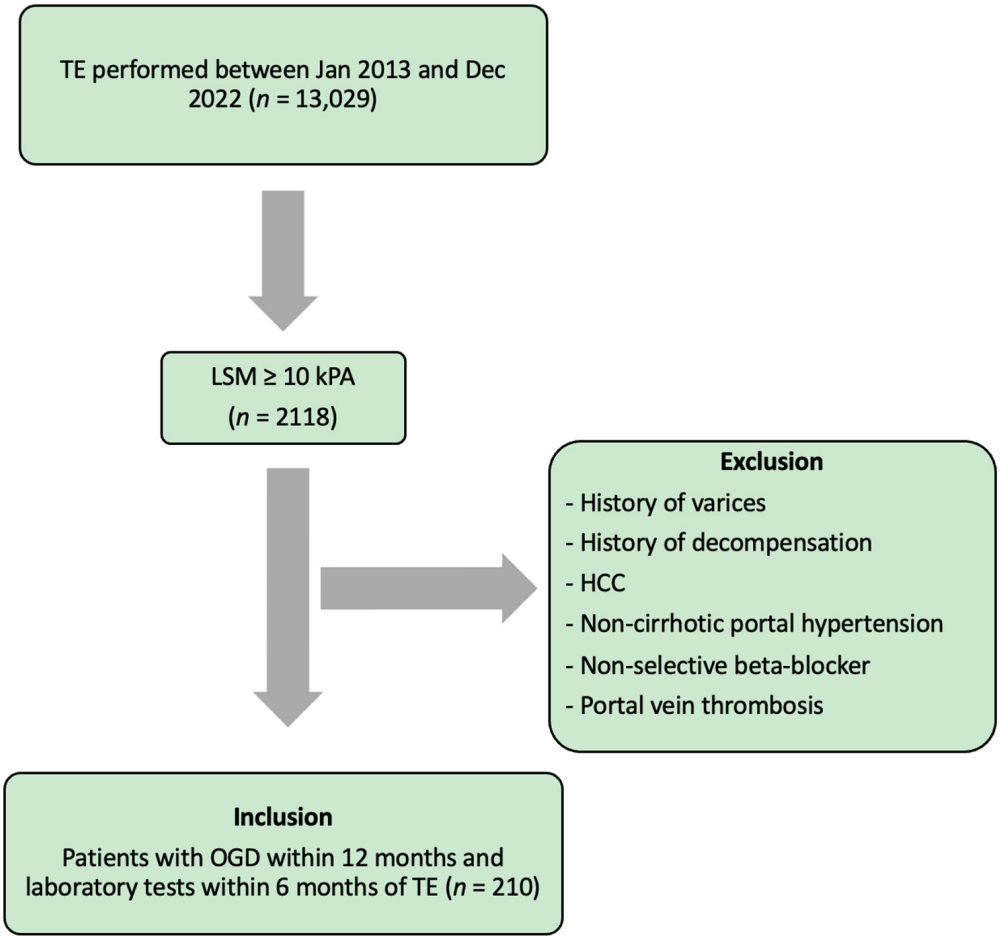

Figure 1. Flow chart of patients included in study.

2.1. Data Collection

Data regarding age, sex, liver disease aetiology, OGD, and TE reports were collected from electronic medical records. Clinical pathology results, i.e., haemoglobin (Hb), white cell count (WCC), platelets (PLT), total bilirubin, albumin, alanine aminotransferase (ALT), aspartate transaminase (AST), sodium (Na), creatinine, urea, international normalised ratio (INR), ferritin (Fe), and alpha-fetoprotein (AFP) were also collected.

2.1.1. Transient Elastography

All TEs were performed using FibroScan® (Echosens, Paris, France) by experienced operators on patients who had fasted for at least 2 h, as per the manufacturer's recommendations. All patients were examined with the right lobe of the liver accessed by the patient lying in a supine position with the right arm fully abducted. The probe tip was placed in the 9th to 11th intercostal spaces with a minimum of ten valid measurements recorded and a median LSM value (kPa) generated. Only examinations that satisfied the quality criteria established by the manufacturer were included. To ensure the validity of the LSM, a minimum success rate of 60% and an interquartile ratio (IQR) not exceeding 30% of the median LSM value were required.

2.1.2. Calculation of NIT Indices

NIT indices were calculated based on their original formulae, as follows:

- FIB-4 [20] = (age [years] × AST [U/L])/(PLT [10^9/L] × ALT [U/L]$^{1/2}$)
- APRI [21] = ((AST [U/L]/ULN)/PLT [×10^9/L])) × 100

- MELD [18] = 0.957 × Log_e(creatinine [mg/dL]) + 0.378 × Log_e(bilirubin [mg/dL]) + 1.120 × Log_e(INR) + 0.643
- MELD-Na [19] = MELD − Na − 0.025 × MELD × (140 − Na) + 140
- FIPS [16] = 1.43 × log10 (bilirubin [mg/dL]) − 1.71/(creatinine [mg/dL]) + 0.02 × (age [years]) − 0.02 × (albumin [g/L])
- EVendo [15] = ((8.5 × INR + AST [U/L]/35)/(PLT [$\times 10^3/\mu$L]/150) + (blood urea nitrogen [mg/dL]/20) + (Hb [g/dL]/15)) + 1 if ascites present
- B6C for excluding HRVs was used as described in the Baveno VI consensus (PLT > 150 × 10^9/L and LSM < 20 kPa) [11].
- E6BC was used as proposed by Augustin et al. (PLT > 110 × 10^9/L and LSM < 25 kPa) [12].

2.1.3. Assessment of Varices

The clinical standard of care in our institutions is for all patients with newly diagnosed liver cirrhosis (defined as a LSM ≥ 10 kPa) to undergo screening OGD within one year of diagnosis. OGD was performed according to standard clinical practice by trained gastroenterologists. Gastroesophageal varices were graded according to the Sarin classification and defined as either low-risk varices (LRVs) or high-risk varices (HRVs). Grade 1 varices were classified as low risk. High risk varices included Grade 2, Grade 3, gastric varices, and any varix with a red wale sign.

2.2. Statistical Analyses

Baseline demographic, aetiological, laboratory, TE, and endoscopy data were systematically collected using a standardised proforma. Data were analysed using IBM SPSS software version 29.0.1.0 (IBM Corp, New York, NY, USA). The Shapiro–Wilk test was used to determine if the numerical variables had a normal distribution. Student's *t*-test was used to compare numerical variables that were normally distributed, while the Mann–Whitney U test was used for those that were not. Normally distributed variables were age and urea meanwhile not normally distributed variables were Hb, WCC, PLT, bilirubin, albumin, ALT, AST, Na, creatinine, INR, Fe, and AFP. The chi-square test was used to compare categorical variables between groups. Logistic regression was used to analyse the independent associations of different parameters with HRVs, and all variables found to be significant in the univariable analysis were included in a multivariable logistic regression analysis.

ROC curves were generated to evaluate the performance of the non-invasive markers for predicting HRVs and the maximum Youden's index was used for estimation of the best cut-off value. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated and expressed with 95% confidence intervals (CI). The level of statistical significance was set to $p < 0.05$. The spared OGD rate was calculated as the ratio of the numbers of patients with OGD that could be spared to the total number of patients. The missed HRV rate was defined by the rate of patients with missed HRVs among the patients who were spared an OGD.

3. Results

3.1. Baseline Characteristics

Of the 210 patients who underwent screening OGD, HRVs were present in 26 (12.4%). 65.7% of all patients were male with median age of 57 years. Most patients (91.9%) were classified as Child–Pugh A and the leading causes of cACLD was hepatitis C virus infection (41.9%), followed by non-alcoholic fatty liver disease (31.4%) and alcohol-related liver disease (15.7%). Patients with HRVs were found to have lower PLT, Hb, and WCC figures. They also had higher bilirubin and INR values. The median LSM was 20.25 kPa, and there was no significant difference between patients with and without HRVs. The baseline demographics and clinical characteristics are summarised in Table 1.

Table 1. Baseline characteristics of study cohort (n = 210).

	All Patients (n = 210)	**No HRVs (n = 184)**	**HRVs (n = 26)**	***p* Value**
Age (years)	57 (49–64)	57 (49.25–64)	58.5 (48.5–62.25)	0.809
Male, *n* (%)	138 (65.7)	118 (64.1)	20 (76.9)	0.198
Aetiology, *n* (%)				0.578
ALD	33 (15.7)	29 (15.8)	4 (15.4)	
NAFLD	66 (31.4)	55 (29.9)	11 (42.3)	
HBV	12 (5.7)	12 (6.5)	0 (0)	
HCV	88 (41.9)	78 (42.4)	10 (38.5)	
Other	11 (5.3)	10 (5.4)	1 (3.8)	
LSM (kPA)	20.25 (12.8–32.45)	19.9 (12.83–31.1)	25.2 (12.65–35.3)	0.551
Hb (g/L)	140.5 (124.75–150.25)	145.5 (126.75–151)	140 (119–154.5)	**0.023**
WCC ($\times 10^9$/L)	5.9 (4.4–7.6)	5.95 (4.375–7.675)	4.3 (3.8–5.9)	**0.017**
PLT ($\times 10^9$/L)	149.5 (91.25–202.25)	135 (79.75–181.75)	89 (61–124.5)	**<0.001**
Bilirubin (μmol/L)	12 (8–20)	10 (8.25–15.75)	16 (12–28)	**0.004**
Albumin (g/L)	37 (34–40)	38 (36–39.75)	35 (29–38)	0.128
ALT (U/L)	46 (29–77)	54.5 (35.25–86.75)	43 (34.5–84)	0.988
AST (U/L)	44 (30–79)	44 (34.75–78.75)	75 (42.5–106.5)	0.406
Na (mmol/L)	139 (138–141)	139 (138–140)	140 (136.5–141)	0.415
Creatinine (μmol/L)	64 (55–76)	64 (55–76.5)	63 (50–68)	0.207
Urea (mmol/L)	4.5 (3.4–5.8)	4.8 (3.7–6.25)	3.8 (2.6–4.85)	0.743
Fe (μg/L)	115 (46.5–311)	112.5 (50.25–319)	206 (35–260)	0.897
INR	1.1 (1–1.2)	1.1 (1–1.2)	1.2 (1.05–1.25)	**0.009**
AFP (IU/mL)	3 (2–7)	3 (2–6.75)	6 (3–7.5)	0.150
Child–Pugh Class, *n* (%)				0.492
A	193 (91.9)	170 (92.4)	23 (88.5)	
B	17 (8.1)	14 (7.6)	3 (11.5)	

Data presented as median values with interquartile range (IQR) or as *n* (%). Abbreviations: HRVs = high risk varices; ALD = alcohol-related liver disease; NAFLD = non-alcoholic fatty liver disease; HBV = hepatitis B; HCV = hepatitis C; LSM = liver stiffness measurement; Hb = haemoglobin; WCC = white cell count; PLT = platelet count; ALT = alanine aminotransferase; AST = aspartate transaminase; Fe = ferritin; INR = international normalised ratio; AFP = alpha-fetoprotein; IU = international units. Bold represents significant *p* values.

The results of a univariable logistic regression analysis revealed a correlation between HRV and WCC (p = 0.006), PLT (p < 0.001), and bilirubin (p = 0.032). However, when a multivariable logistic regression analysis was conducted, only PLT remained as a significant independent predictor for HRV (Table 2).

Table 2. Logistic regression model for prediction of high-risk varices.

Variable	**Univariate Analysis**				**Multivariate Analysis**			
	β	**OR**	**95% CI**	***p* Value**	**β**	**OR**	**95% CI**	***p* Value**
WCC	−0.476	0.621	0.477–0.808	<0.001 *				
PLT	−0.019	0.981	0.972–0.990	<0.001 *	−0.019	0.981	0.972–0.990	<0.001 *
Bilirubin	0.036	1.037	1.003–1.072	0.032				

* Indicates significance, with $p < 0.05$. Abbreviations: β = β coefficient; OR = odds ratio; CI = confidence interval; WCC = white cell count; PLT = platelet count.

3.2. Performance and Safety of the NITs in Patients with cACLD

Comparison between ROC curves of the various NITs are depicted in Figure 2.

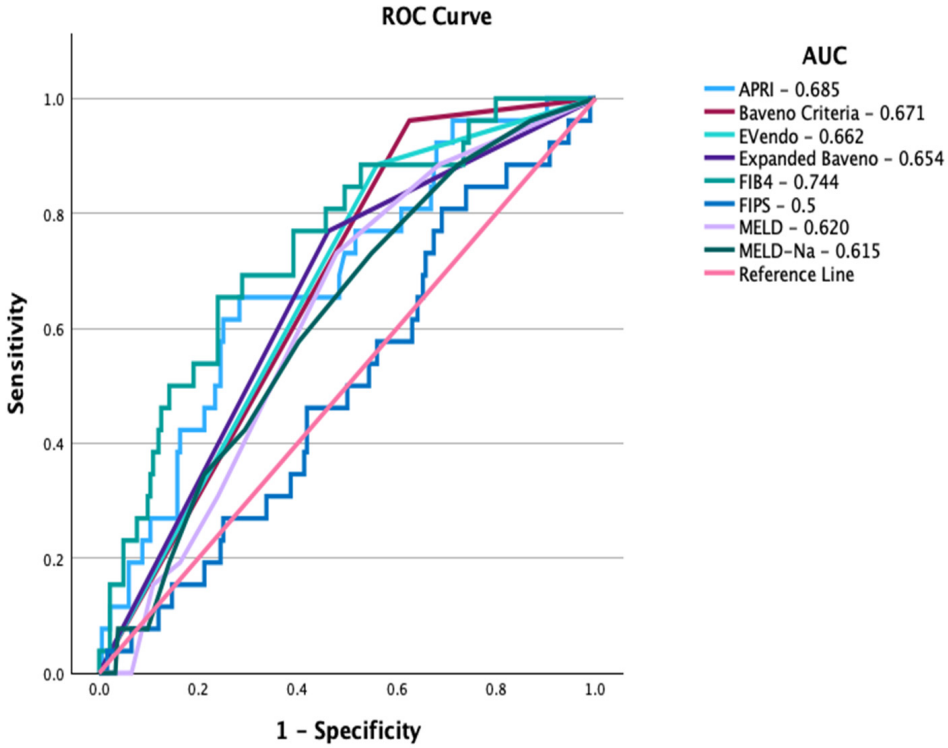

Figure 2. Comparison of ROC curves between NITs. The NITs were assessed for their capability to bypass OGD screening without missing any HRVs, using cut-off values from the ROC curves generated or established criteria. The AUROC was highest for the FIB-4 score (0.744, $p < 0.001$). The AUROC for the FIPS score was 0.5 and did not reach statistical significance ($p = 0.988$).

The area under the ROC curve (AUROC) was greatest for the FIB-4 score 0.744 ($p < 0.001$). The NITs were next evaluated for their ability to avoid screening OGD without missing any HRVs. The calculations were based on cut-off values obtained from the ROC curves or from previously established criteria (B6C, EB6C, and EVendo). The AUROC for the FIPS score was 0.5 and therefore not possible to identify a cut-off for predicting HRVs. The performances of all NITs in predicting any HRVs are described in Tables 3 and 4, respectively.

Table 3. Performance of non-invasive tests in predicting high-risk varices.

	Cut-Off	AUC	Sensitivity	Specificity	PPV	NPV	+LR	−LR
Baveno VI	PLT > 150 and LSM < 20	0.671	96.2	38	18	98.6	1.55	0.1
Expanded Baveno	PLT > 110 and LSM < 25	0.654	76.9	53.8	19	94.3	1.66	0.43
FIB4	4.409	0.744	65.4	76.1	27.9	94	2.74	0.45
APRI	1.372	0.685	65.4	71.7	24.6	93.6	2.31	0.48
FIPS	−2.762	0.5	80.8	31	14.2	91.9	1.17	0.62
MELD	7.5	0.620	73.1	52.2	17.8	93.2	1.53	0.52
MELD-Na	8.5	0.615	73.1	45.1	15.8	92.2	1.33	0.6
EVendo	3.9	0.662	88.5	44	18.3	95.4	1.58	0.26

Table 4. Performance of non-invasive tests for screening oesophagogastroduodenoscopy.

	Cut-Off	Spared OGD (%)	Missed HRVs (%)
Baveno VI	PLT > 150 and LSM < 20	33.8	1.41
Expanded Baveno	PLT > 110 and LSM < 25	50	5.71
FIB4	4.409	71	6.04
APRI	1.372	67.1	6.38
FIPS	−2.762	29.5	8.06
MELD	7.5	49	6.8
MELD-Na	8.5	42.8	7.77
EVendo	3.9	40	3.57

The B6C had the highest sensitivity and NPV while the FIB-4 had the highest specificity, PPV, and positive likelihood ratio (LR). OGDs could be circumvented for 33.8% of patients using the B6C (HRV miss rate 1.4%), 50% for patients using the EB6C (HRV miss rate 5.7%), 71% for patients using the FIB-4 score (HRV miss rate 6%), 67.1% for patients using the APRI score (HRV miss rate 6.4%), 49% for patients using the MELD score (HRV miss rate 6.8%), 42.8% for patients using the MELD-Na score (HRV miss rate 7.7%), and 40% for patients using the EVendo score (HRV miss rate 3.6%). Compared to the B6C, all other NITs were able to spare more endoscopies although only the EVendo score was able to maintain a HRV miss rate of <5%.

3.3. Performance and Safety of B6C and EVendo in cACLD Subgroups

Considering B6C and EVendo were the only NITs with acceptable HRV miss rates, we conducted subgroup analysis to evaluate their efficacies among the various aetiologies of cACLD. The findings are summarised in Table 5.

Table 5. Performance and safety of B6C and EVendo in compensated advanced chronic liver disease subgroups.

	Spared OGD (%)		Missed HRVs (%)	
	B6C	**EVendo**	**B6C**	**EVendo**
HBV	50% (6/12)	50% (6/12)	0% (0/6)	0% (0/6)
HCV	31.8% (28/88)	30.7% (27/88)	0% (0/28)	0% (0/27)
ALD	21.2% (7/33)	30.3% (10/33)	0% (0/7)	0% (0/10)
NAFLD	43.9% (29/66)	56.1% (37/66)	3.4% (1/29)	8.1% (3/37)
Other	9.1% (1/11)	36.4% (4/11)	0% (0/1)	0% (0/4)

In the HBV cohort, 50% of patients avoided OGDs (HRVs were not missed in any case) with either B6C or EVendo. For the HCV group, OGDs were avoided by 31.8% and 30.7% of patients (HRVs were not missed in any instance) with the use of B6C and EVendo, respectively. Within the ALD subgroup, OGDs were spared for 21.2% and 30.3% of patients (HRVs were not missed in any case) with B6C and EVendo, respectively. In the NAFLD category, OGDs were avoided by 43.9% and 56.1% of patients (HRVs were missed in 3.4% and 8.1% of cases, respectively) with B6C and EVendo. Finally, in the "other group", OGDs were spared for 9.1% and 36.4% of patients (HRVs were not missed in any instance) with B6C and EVendo, respectively.

4. Discussion

Our study compared the performance of several NITs, and we validated the use of the B6C in predicting HRVs across all aetiologies of cACLD in a real-world Australian clinical

setting. Given that oesophageal varices are a common and potentially life-threatening complication of liver cirrhosis, the importance of early identification of HRVs to initiate prompt prophylaxis against acute variceal bleeding in patients with cACLD cannot be overstated. Accordingly, there is a growing interest in the use of NITs to accurately predict the presence of these HRVs, thereby obviating the need for screening OGD. This is especially relevant in current times following the COVID-19 pandemic with endoscopy units worldwide still recovering from a backlog of cases following reductions in elective procedures [22].

The prevalence of HRVs in our cohort was 12.4%, which is comparable to data from several similar studies as demonstrated by Stafylidou et al. [17]. PLT remained the only independent risk factor for the presence of HRVs after multivariable logistic regression analysis. This is likely explained by the fact that worsening thrombocytopaenia is due to platelet sequestration seen in congestive splenomegaly which results from rising portal pressures. A study by Chen et al. also found that PLT was one of the variables used in identifying patients who could avoid screening OGD for varices [23].

As with the meta-analysis by Stafylidou et al., our study found that the B6C had a low specificity of 38%, which resulted in a low spared OGD rate of 33.8%. The B6C in our study, however, demonstrated a high NPV and low negative LR at the expense of poor PPV and positive LR with similar findings from several other studies worldwide [24–27]. These results support the notion that the B6C is better as a screening tool in excluding HRV rather than diagnosing them.

Regarding spared OGDs, it is considered acceptable to miss less than 5% of HRVs as per the Baveno VI consensus guidelines [11]. Assuming this recommendation, the EVendo score could safely spare the highest number of OGDs, followed by the B6C. The FIB-4 scored the highest AUC and could spare the greatest number of OGDs. A possible reason is because the FIB-4 has been proven to be accurate in assessing liver fibrosis in patients with hepatitis C, which represents the majority of patients in our study [28]. However, its use comes with an unacceptable HRV miss rate of 6%.

Given that the B6C and EVendo scores demonstrated the best safety profile among all the scores, we further analysed the efficacy of these NITs across all aetiologies of cACLD. The pertinent finding was that missed HRVs were seen solely in NAFLD patients, and more so in the EVendo group. Interestingly, Alswat et al. were able to successfully validate the EVendo score in their cohort of 103 patients in Saudi Arabia with a HRV miss rate of only 1.7% compared to 3.6% in our cohort [29]. However, an important factor to note was that they did not reveal which cirrhosis aetiologies were implicated in HRV misclassification. Additionally, their study only included 20 NAFLD patients, less than a third of those in our cohort. A possible reason behind the EVendo score's inaccuracy in NAFLD patients is that it incorporates the presence of ascites in its formula which may be challenging to detect particularly in these patients who are often obese and have a high waist circumference. Further studies are warranted to assess the validity of the EVendo score in a larger cohort of NAFLD patients.

In our study, the B6C misclassified only one patient as having no HRVs. On closer analysis, this patient had narrowly met the B6C with a borderline PLT and as per current Baveno VII recommendations, he would have had his PLT and LSM measurements repeated the following year [30]. He would then have fallen out of criteria due to a worsening PLT and subsequently would have been referred for screening OGD. Hence, annual measurements of PLT and LSM represent a reasonable safety model to prevent HRVs from going undetected before decompensation with variceal bleeding. The main criticism of the B6C is its poor specificity and hence low spared OGD rate, leading to up to 40% of OGDs performed in cACLD patients being unnecessary [17,31]. This drawback led to the development of the E6BC which was described to almost double the spared OGD rate from 21% to 40% with a low missed HRV rate of 1.6% [12]. Although the E6BC was able to spare up to 50% of OGDs in our cohort, it missed an unacceptable number of HRVs (5.7%).

We are the first to evaluate and compare the performances of various NITs in an adult Australian population. We also included a diverse cohort of well, compensated patients

with a low pre-test probability of having HRVs (majority of them being Child–Pugh A), making it applicable and practical in an outpatient clinical setting. Another strength of our study was the exclusion of patients with known varices, which was not a feature among other similar studies. This is pertinent as international guidelines recommend surveillance OGD every 1–2 years for patients with known small varices, thereby making non-invasive screening in this population not applicable [32,33]. Additionally, another feature which sets our study apart was that we also sought to exclude patients who were already on NSBB therapy. This ties in with the current Baveno VII recommendations of foregoing screening endoscopy for varices in patients with cACLD who are already on NSBB therapy to prevent any hepatic decompensation [30].

Our study has some limitations. Due to its retrospective nature, the results may have been affected by selection bias. Secondly, OGDs and LSMs were performed by various operators across different institutions and therefore, the presence of inter-observer variability cannot be excluded.

In conclusion, our findings support the efficacy of the B6C in predicting HRVs in a real-world cohort of cACLD patients in Australia. Using the B6C in the right clinical context enables us to omit screening OGD for 33.8% of cACLD patients with a high sensitivity of 96.2% and negative predictive value of 98.6% for ruling out HRVs. The use of the B6C in regular clinical practice is safe and dependable in cACLD patients.

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Informed Consent Statement: Patient consent was waived because this study is retrospective, and the data were obtained from a secure database with anonymised information.

Data Availability Statement: All the supporting data concerning the study are available and can be obtained from the corresponding authors upon reasonable request.

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