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Article

External Validation of The Hospital Frailty Risk Score (HFRS) to Identify Liver Cirrhosis Patients at Risk for Frailty Mortality: A Multi Centre Retrospective Cohort Study in Asians

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Abstract

Background/Objectives: Frailty is a well-established predictor of adverse outcomes in older adults and patients with chronic disease. The Hospital Frailty Risk Score (HFRS), derived from administrative ICD-10 data, was previously developed and validated in Western populations to identify frailty risk. This study aimed to validate the HFRS in an Asian cirrhotic population and evaluate its ability to predict mortality and hospital readmissions. **Methods:** Patients with liver cirrhosis and at least one hospital admission in 2018 from two tertiary public hospitals in Singapore were identified using ICD-10 codes. HFRS was calculated using a two-year lookback period according to Gilbert's methodology. Patients were categorized as no risk (score = 0), low risk (score < 5), intermediate risk (5–15), or high risk (>15). Outcomes assessed included 30-day mortality, 30-day hospital readmission, and 2-year mortality, with follow-up until 31 December 2020. Multivariate logistic regression analysis was performed. **Results:** A total of 814 patients were included, of whom 629 (77.3%) had frailty-related ICD-10 codes. Increasing HFRS category was independently associated with worse outcomes. Compared with the reference group, 30-day mortality increased stepwise with frailty: low risk odds ratio (OR) 25.74 (95% CI 1.54–431.33, p = 0.02), intermediate risk OR 40.42 (95% CI 2.42–676.14, p = 0.01), and high risk OR 50.92 (95% CI 2.92–887.08, p < 0.01). Higher HFRS was also associated with increased 30-day readmission and 2-year mortality across all risk categories. **Conclusions:** Frailty-related diagnoses are significant independent predictors of mortality and hospital readmission in patients with liver cirrhosis. HFRS is a cost-effective and scalable tool using administrative data to identify high-risk patients and support clinical risk stratification.

Keywords: frailty; liver cirrhosis; Hospital Frailty Risk Score; mortality; ICD-10

1. Introduction:

Frailty is most often defined as an aging-related syndrome of physiological decline, characterized by marked vulnerability to adverse health outcomes. It is a multifaceted concept involving physical, psychological, social, and environmental factors[1]. The cumulative decline depletes homeostatic reserves such that minor stressor events trigger disproportionate changes in health status and thus contribute to an increased risk of institutionalization and death. [2] While

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originally coined as a geriatric condition, frailty is present in patients with serious or life limiting illnesses such as liver cirrhosis, regardless of age.

There are several reasons why patients with liver cirrhosis are at higher risk of frailty.

Cirrhosis is a catabolic state of an imbalance between energy needs and intake with accelerated muscle breakdown.[3] The presence of portosystemic shunts and liver metabolic dysfunction leads to increased ammonia in the blood which is myotoxic.[4] In addition, complications of cirrhosis such as hepatic encephalopathy and ascites lead to anorexia, early satiety and reduced protein intake. Physical activity is also reduced. This directly correlates to frailty and increased mortality risk [5].

Validated tools to assess frailty in liver cirrhosis such as the Fried Frailty Index (FFI), Liver Frailty Index (LFI) and the Clinical Frailty Scale (CFS) [1], all largely focus on physical frailty. In addition, both FFI and LFI require physical function testing. FFI requires physical measures such as walking speed and grip strength[6]. LFI, although specifically designed for liver patients with good prediction of liver transplant waitlist mortality, requires assessment of hand grip strength, chair stands, and position balance [7]. In real world clinical practice, unless patients are enrolled into a multidisciplinary programme or research study, these tests can be difficult to perform routinely in a busy ambulatory setting. The CFS classification is based on descriptors and labels at various levels of frailty with an attached visual chart to assist [8]. While it is easier and less time consuming to administer, the focus is still on physical frailty and CFS is a single global score lacking detail which is unhelpful for tracking patient progress for specific functions over time.

The Hospital Frailty Risk Score (HFRS) was more recently developed and externally validated to identify frailty at a population level. HFRS has been shown to perform as well or even better than existing frailty or risk stratification tools such as FFI and Rockwood Frailty Index [9–12] . HFRS is a score derived from weighted International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) codes of frailty related diagnoses. The frailty related diagnoses include mobility issues, falls, fractures, pressure ulcers, incontinence, cognitive impairment, anxiety, depression and functional dependence. Patients are categorized as low risk (<5), intermediate risk (5-15), and high risk (>15). Patients with higher scores had 70% higher risk of mortality at 30 days, were 6 times more likely to have longer hospital stays and were 50% more likely to be readmitted within 30 days [12]**.** HFRS was originally derived from a western geriatric population of patients aged more than 75 years old.

This study aims to validate HFRS in an Asian population, particularly as a tool to identify patients with cirrhosis at risk of frailty and to predict 30 -day mortality, 30-day readmission and 2 year mortality after adjusting for age and disease severity.

2. Methodology

2.1. Study Population and Design

This is a multi-centre, retrospective cohort study. Patients with liver cirrhosis who had at least 1 hospital admission from January to December 2018 at 2 large tertiary public hospitals in Singapore were identified using ICD-10 codes. Liver cirrhosis was confirmed via chart review either through imaging, elastography or histology results. Patients with lab tests done for creatinine, total bilirubin and either prothrombin time or international normalized ratio (for MELD score calculation) within 180 days of their first inpatient admission were selected for the study. All research was conducted in accordance with both the Declarations of Helsinki and Istanbul and was approved by the Singhealth institutional review board with waiver of informed consent.

2.2. HFRS Calculation and Risk Stratification

A 2-year lookback period, as utilized in the original HFRS study by *Gilbert et al*, was used to identify presence of frailty related ICD-10 diagnoses. Various weightage was applied to different frailty related diagnostic codes as detailed in the original paper [12] with the HFRS calculated using the cumulative sum of weighted ICD-10 codes. Patients were categorized into 4 distinct groups: no

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risk (HFRS = 0, reference group), low risk (0<HFRS <5), intermediate risk (HFRS 5-15) or high risk (HFRS >15).

Outcome data were collected through systematic review of electronic medical records up to 31st December 2020, ensuring a minimum potential follow-up of 2 years for all patients. The primary outcome was all-cause mortality at 30 days from index admission date and non-elective readmissions within 30 days. The secondary outcome was all-cause mortality at 2 years from index admission date. Patients were followed up until death or censored at 2 years (730 days) from index admission, whichever occurred first. Key factors analysed included: HFRS categories, MELD score at index admission, age categories and etiology of liver disease

2.3. Statistical Analysis

Normality of data was assessed by Shapiro-Wilk normality test. Categorical variables were expressed as frequencies and percentages and compared using the Pearson's Chi-squared test or Fisher's exact test as appropriate. Continuous variables were presented as median with interquartile range (IQR) and analysed using Kruskal-Wallis rank sum test. For the primary and secondary outcomes, logistic regression was performed to determine associated predictors of 30-day and 2-year mortality and 30-day hospital readmissions. Variables with p-value ≤0.10 in the initial univariate analysis were considered potential risk factors and included in the multivariate model. For the multivariate logistic regression analysis, we established these additional reference categories for other variables:

- Etiology: MASLD served as the reference category
- Age: Below 65 years was set as the reference category
- MELD score: Scores below 11 were designated as the reference category
- HFRS: No risk group (HFRS=0) was the reference category

The OR for each category were calculated in comparison to their respective reference categories. For the categorical variables, only the comparison groups' ORs were reported, with the reference category (OR=1) serving as the baseline for interpretation. The multivariate model was adjusted for potential confounders including age category and MELD score. Adjusted odds ratios (aOR) with 95% confidence intervals were calculated to evaluate the independent association of HFRS with outcome. P-value ≤0.05 was considered statistically significant in the multivariate analysis. All logistic regression models were built using Bias Reduction in Binomial-response Generalized Linear Models.

Likelihood ratio test was conducted to compare whether a model with only age and MELD score as predictors for 2-year mortality or a model with HFRS, age and MELD score as predictors for 2-year mortality would provide a better fit. Statistical analysis was performed using R studio (version 4.3.1).

3. Results

A total of 1016 patients with liver cirrhosis with at least one admission in 2018 were identified via electronic health records. Of these, 814 patients had available laboratory data for creatinine, total bilirubin and either prothrombin time or international normalised ratio within 180 days of their index admission and were included in the study. Among them, 629 patients had visits coded with frailty related ICD-10 diagnoses. Based on the Hospital Frailty Risk Score (HFRS), 315 patients (50.1%) were classified as low risk, 228 (36.2%) as intermediate risk, and 86 (13.7%) as high risk (Figure 1).

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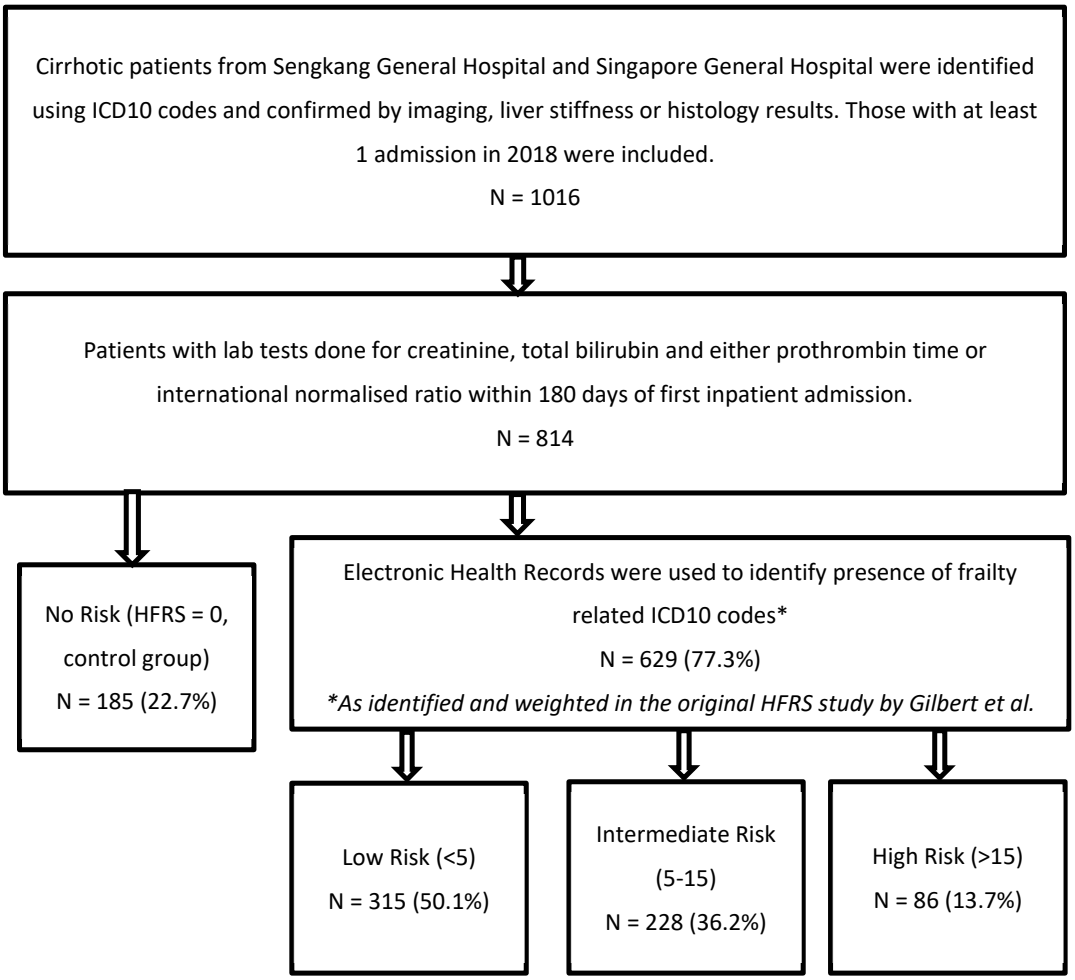


Figure 1. Flowchart.

3.1. Baseline Characteristics

The median age of the cohort was 66 years (IQR 59–74). Most patients were of Chinese ethnicity (76.3%) and male (65.1%). Metabolic dysfunction associated fatty liver disease (MASLD) was the most common etiology of cirrhosis (34.8%), followed by hepatitis B (29.7%) and alcohol-related disease (11.9%) (Table 1). Laboratory values also worsened with increasing frailty: bilirubin, creatinine, and INR rose significantly across HFRS categories (all $p < 0.01$)

Table 1. Baseline Characteristics.

Baseline Characteristics	Total (n=814)	No Risk (n=185)	Low Risk (n=315)	Intermediate Risk (n=228)	High Risk (n=86)	P-value
Gender						
Female	284 (34.9)	64 (34.6)	108 (34.3)	82 (36.0)	30 (34.9)	0.98
Male	530 (65.1)	121 (65.4)	207 (65.7)	146 (64.0)	56 (65.1)	
Age at first visit in 2018 (median (IQR))	66.00 (59.25-74.00)	66.00 (60.00-73.00)	66.00 (60.00-73.00)	67.50 (59.75-76.25)	67.00 (58.00-76.00)	0.36
Race						
Chinese	621 (76.3)	139 (75.1)	246 (78.1)	176 (77.2)	60 (69.8)	0.42
Malay	54 (6.6)	11 (5.9)	18 (5.7)	18 (7.9)	7 (8.1)	0.69
Indian	68 (8.4)	9 (4.9)	25 (7.9)	20 (8.8)	14 (16.3)	**0.02**

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Others	71 (8.7)	26 (14.1)	26 (8.3)	14 (6.1)	5 (5.8)	**0.02**
Etiology						
MASLD	283 (34.8)	86 (46.5)	92 (29.2)	80 (35.1)	25 (29.1)	**<0.01**
Hepatitis B	242 (29.7)	42 (22.7)	121 (38.4)	63 (27.6)	16 (18.6)	**<0.01**
Hepatitis C	49 (6.0)	10 (5.4)	15 (4.8)	16 (7.0)	8 (9.3)	0.38
Alcohol	97 (11.9)	14 (7.6)	35 (11.1)	29 (12.7)	19 (22.1)	**<0.01**
Autoimmune disease	45 (5.5)	13 (7.0)	16 (5.1)	13 (5.7)	3 (3.5)	0.69
Cardiac	25 (3.1)	2 (1.1)	6 (1.9)	12 (5.3)	5 (5.8)	**0.02**
Cryptogenic	37 (4.5)	9 (4.9)	14 (4.4)	8 (3.5)	6 (7.0)	0.58
Others*	14 (1.7)	3 (1.6)	8 (2.5)	2 (0.9)	1 (1.2)	0.59
>1 etiology	22 (2.7)	6 (3.2)	8 (2.5)	5 (2.2)	3 (3.5)	0.83
Lab Test Results						
Total Bilirubin (umol/L) (median (IQR))	20.00 (12.00-38.00)	18.00 (12.00-28.00)	19.00 (12.00-35.50)	25.50 (14.00-42.25)	21.00 (13.00-40.75)	**<0.01**
Creatinine (umol/L) (median, IQR)	79.25 (63.00-111.00)	74.00 (60.00-87.00)	77.00 (62.50-96.00)	95.00 (68.00-153.60)	116.50 (72.25-228.00)	**<0.01**
International Normalised Ratio (median,IQR)	1.14 (1.07-1.28)	1.11 (1.05-1.22)	1.12 (1.07-1.25)	1.20 (1.09-1.35)	1.21 (1.10-1.45)	**<0.01**

*Rare causes including Wilson's, Haemochromatosis, Alpha1 antitrypsin deficiency, etc.

3.2. 30-day Mortality

Increasing HFRS was associated with higher 30-day mortality compared with non-frail patients (Figure 2a). No patients suffered 30-day mortality in the no-risk (HFRS=0) group, compared to 11.6% (10/86) in the high risk (HFRS >15) group (Supp Table 2). Firth's bias reduction method was applied with penalized logistic regression, in view of zero event data. 30-day mortality risks in HFRS categories were as such: Low risk, OR 25.74 (1.54 - 431.33), p=0.02; intermediate risk, OR 40.42 (2.42 - 676.14), p =0.01; and high risk OR 50.92 (2.92 - 887.08), p<0.01. Subsequent multivariate analysis was performed with adjustment for age and MELD score. Adjusted odds ratios (aORs) for 30-day mortality risk were: low risk, aOR 20.57 (1.26 - 334.91), p = 0.03; intermediate risk, aOR 20.01 (1.22 - 329.43) p = 0.01; and high risk, aOR 22.65 (1.31 - 390.49) p =0.03). MELD scores >11 were also independently associated with higher risk of 30-day mortality (Table 2).

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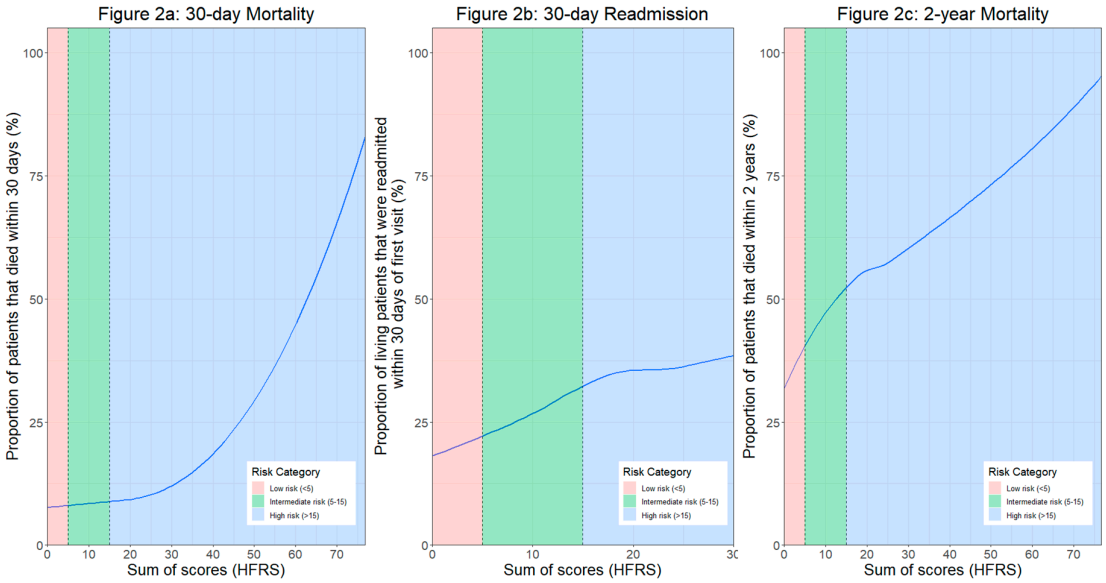


Figure 2. Primary and Secondary Outcomes.

Table 2. Univariate and Multivariate Analysis for 30-days mortality.

	Univariate Analysis		**Multivariate Analysis**	
Parameters	**Odds Ratio (OR, 95% CI)**	**P-value**	**Adjusted Odds Ratio (aOR, 95% CI)**	**P-value**
Etiology of Liver disease		0.51		
MASLD/NASH (reference)	1			
Hepatitis B	1.79 (0.85 - 3.75)	0.12		
Hepatitis C	2.15 (0.69 - 6.66)	0.19		
Alcohol	2.33 (0.97 - 5.62)	0.06		
Autoimmune Disease	1.25 (0.31 - 5.10)	0.76		
Cardiac	2.31 (0.54 - 9.81)	0.26		
Cryptogenic	2.92 (0.93 - 9.19)	0.07		
Others	2.41 (0.38 - 15.14)	0.35		
>1 etiology	0.48 (0.03 - 8.96)	0.63		
Frailty risk category		**<0.01**		**<0.01**
Without any frailty codes (HFRS = 0) (reference)	1		1	
0< HFRS < 5	25.74 (1.54 - 431.33)	**0.02**	20.57 (1.26 - 334.91)	**0.03**
HFRS 5 to 15	40.42 (2.42 - 676.14)	**0.01**	20.01 (1.22 - 329.43)	**0.04**
HFRS > 15	50.92 (2.92 - 887.08)	**<0.01**	22.65 (1.31 - 390.49)	**0.03**
Age category		0.59		
Below 65 (reference)	1			
65 to 75	0.88 (0.46 - 1.70)	0.71		
Above 75	1.31 (0.66 - 2.61)	0.44		
MELD score		**<0.01**		**<0.01**
Below 11 (reference)	1		1	
11 to 18	3.64 (1.60 - 8.27)	**<0.01**	3.01 (1.33 - 6.85)	**<0.01**
19 to 24	6.94 (2.85 - 16.91)	**<0.01**	5.07 (2.05 - 12.53)	**<0.01**
Above 24	20.41 (7.84 - 53.14)	**<0.01**	14.06 (5.15 - 38.35)	**<0.01**

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3.3. Readmission Within 30 Days of First Visit

Similarly, higher HFRS was associated with greater risk of readmission within 30 days of first visit (Figure 2b). The odd ratios (ORs) were: low risk, OR 1.66 (0.96-2.88) p = 0.07; intermediate risk, OR 3.26 (1.88-5.65) p <0.01 and high risk, OR 4.74 (2.47-9.13) p <0.01. After multivariate analysis with adjustment for age and MELD score, intermediate HFRS scores and above were associated with readmissions within 30 days: intermediate risk aOR 2.83 (1.60 - 4.98), p<0.01; high risk aOR 3.91 (1.98 - 7.72), p<0.01 (Table 3)

Table 3. Univariate and Multivariate Analysis for 30-days Readmission.

	Univariate Analysis		**Multivariate Analysis**	
Parameters	**Odds Ratio (OR, 95% CI)**	**P-value**	**Adjusted Odds Ratio (aOR, 95% CI)**	**P-value**
Etiology of Liver disease		0.90		
MASLD/NASH (reference)	1			
Hepatitis B	0.71 (0.46 - 1.11)	0.14		
Hepatitis C	0.99 (0.47 - 2.10)	0.98		
Alcohol	0.94 (0.53 - 1.68)	0.84		
Autoimmune Disease	0.80 (0.36 - 1.80)	0.59		
Cardiac	0.77 (0.26 - 2.29)	0.64		
Cryptogenic	0.79 (0.32 - 1.97)	0.62		
Others	1.59 (0.48 - 5.26)	0.45		
>1 etiology	1.05 (0.38 - 2.92)	0.92		
Frailty risk category		**<0.01**		**<0.01**
Without any frailty codes (HFRS = 0) (reference)	1		1	
0<HFRS<5	1.66 (0.96 - 2.88)	**0.07**	1.59 (0.91 - 2.76)	0.10
HFRS 5 to 15	3.26 (1.88 - 5.65)	**<0.01**	2.83 (1.60 - 4.98)	**<0.01**
HFRS > 15	4.74 (2.47 - 9.13)	**<0.01**	3.91 (1.98 - 7.72)	**<0.01**
Age category		0.34		
Below 65 (reference)	1			
65 to 75	0.81 (0.54 - 1.21)	0.30		
Above 75	1.14 (0.73 - 1.79)	0.56		
MELD score		**<0.01**		0.25
Below 11 (reference)	1		1	
11 to 18	1.63 (1.09 - 2.43)	**0.02**	1.34 (0.89 - 2.02)	0.16
19 to 24	2.31 (1.37 - 3.91)	**<0.01**	1.58 (0.91 - 2.76)	0.10
Above 24	3.03 (1.34 - 6.85)	**<0.01**	1.86 (0.80 - 4.34)	0.15

3.4. Two-Year Mortality

Frailty was also strongly associated with longer term outcomes. As illustrated in Figure 2c, patients with higher HFRS had significantly increased risk of 2-year mortality: Low risk (OR 1.79 [1.18-2.71], p <0.01), intermediate risk (OR 2.83 [1.84-4.36], p <0.01), high risk (OR 4.25 [2.46-7.35], p <0.01).

After multivariate analysis with adjustment for age and MELD score, the adjusted odd ratios (aORs) for HFRS were: low risk, aOR 1.60 (1.04-2.45, p = 0.03; intermediate risk, aOR 1.85 (1.17-2.93), p <0.01 and high risk, aOR 2.49 (1.39-4.47), p <0.01. (Table 4). Age above 75 years old and MELD scores above 11 were also independent risk factors for 2-year mortality.

A likelihood ratio test was performed between a model without HFRS and a model with HFRS for 2-year mortality. The first model consisted of two predictors: age and MELD score. The second

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model consisted of three predictors: age, MELD score and HFRS. A result of $\chi^2(3) = 11.347$, $p < 0.01$ was obtained, which suggests that the second model, the more complex model with HFRS, has a better fit than the first model, without HFRS.

Table 4. Univariate and Multivariate Analysis for 2-year Mortality.

	Univariate Analysis		Multivariate Analysis	
Parameters	**Odds Ratio (OR, 95% CI)**	**P-value**	**Adjusted Odds Ratio (aOR, 95% CI)**	**P-value**
Etiology of Liver disease		0.15		
MASLD/NASH (reference)	1			
Hepatitis B	1.11 (0.78 - 1.58)	0.56		
Hepatitis C	0.77 (0.40 - 1.48)	0.44		
Alcohol	1.26 (0.79 - 2.02)	0.33		
Autoimmune Disease	0.51 (0.24 - 1.06)	**0.07**		
Cardiac	0.99 (0.42 - 2.31)	0.98		
Cryptogenic	1.81 (0.91 - 3.60)	**0.09**		
Others	0.52 (0.15 - 1.85)	0.31		
>1 etiology	0.83 (0.33 - 2.09)	0.69		
Frailty risk category		**<0.01**		**0.01**
Without any frailty codes (HFRS = 0) (reference)	1		1	
0<HFRS<5	1.79 (1.18 - 2.71)	**<0.01**	1.60 (1.04 - 2.45)	**0.03**
HFRS 5 to 15	2.83 (1.84 - 4.36)	**<0.01**	1.85 (1.17 - 2.93)	**<0.01**
HFRS > 15	4.25 (2.46 - 7.35)	**<0.01**	2.49 (1.39 - 4.47)	**<0.01**
Age category		**<0.01**		**<0.01**
Below 65 (reference)	1		1	
65 to 75	1.08 (0.78 - 1.50)	0.65	1.27 (0.89 - 1.80)	0.19
Above 75	2.19 (1.51 - 3.17)	**<0.01**	2.50 (1.68 - 3.72)	**<0.01**
MELD score		**<0.01**		**<0.01**
Below 11 (reference)	1		1	
11 to 18	2.24 (1.61 - 3.12)	**<0.01**	2.13 (1.51 - 3.00)	**<0.01**
19 to 24	4.15 (2.64 - 6.51)	**<0.01**	3.63 (2.25 - 5.85)	**<0.01**
Above 24	6.07 (3.02 - 12.19)	**<0.01**	5.33 (2.54 - 11.18)	**<0.01**

4. Discussion

In this study, we validated the Hospital Frailty Risk Score (HFRS) in an Asian cohort of patients with cirrhosis. We found that higher frailty index, as measured by HFRS, was independently associated with increased short (30 day) and long term (2 year) mortality as well as higher 30-day readmission rates. High risk patients (HFRS>15) were 23 times more likely to die in 30 days (aOR 22.65 (1.31 - 390.49),p=0.03) and were 4 times more likely to have readmissions within 30 days (aOR 3.91 (1.98 - 7.72), p <0.01) compared to patients without frailty related diagnoses (HFRS=0). These associations remained significant after adjusting for age and cirrhosis disease severity using MELD score, underscoring the usefulness of HFRS as a frailty tool in cirrhosis.

Our findings show a congruent trend with existing literature on HFRS in cirrhosis. The HFRS has been shown to correlate with increased mortality risk in patients with heart failure, stroke and critical care. [9,11,13] For patients with liver disease, a study by Shah et al, demonstrated that increasing HFRS was associated with a significantly increased odds of acute on chronic liver failure (ACLF) hospitalization versus non-ACLF hospitalization (OR 1.03 per score point, 95% CI 1.02–1.03, p <0.001). This was associated with poorer long-term survival from the time of hospitalization (HR

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1.02 per 5 score points, 95% CI 1.01–1.04, p = 0.004) [14]. A second study by Mahmud et al, looked at HFRS and post-operative mortality risk in patients with liver cirrhosis undergoing major surgery. This study also demonstrated that increasing frailty category was associated with poorer post-operative survival (HFRS >15; HR 1.74, 95% CI 1.05-2.88, p=0.032) [15]. However, both studies were conducted in largely Caucasian populations and were not adjusted for age. Our study evaluated a multi-ethnic Asian population and confirms that HFRS retains prognostic value even after adjustment for both age and MELD score for both early and late outcomes. Of note, our findings showed higher than expected aORs for 30-day mortality compared to available literature. This could be partly explained by zero event data in the no risk (HFRS=0) group where none of the patients had 30-day mortality compared to frail patients. Statistical methods such as Firth's bias reduction with penalized logistic regression were utilized to correct for zero event data. But we acknowledge that larger cohort data without zero event groups is needed in future studies to improve the accuracy of our findings, specifically for 30-day mortality. Overall, we report similar results that higher frailty scores were associated with substantially increased odds of 30-day mortality, readmission rate, and 2-year mortality, thus highlighting the vulnerability of frail cirrhotic patients during and immediately after hospitalisation and in the longer term over 2 years.

HFRS, an easily calculable score, has the potential to quickly identify at-risk patients for additional interventions. HFRS could be automatedly calculated and implemented into the electronic health record and removes the additional "clinical burden" of manual scoring systems. We envision that the HFRS can be added to existing clinical dashboards, especially for patients with cirrhosis. It has the ability to screen the majority of liver cirrhosis patients whereas tools such as LFI and FFI, while well-validated, require physical testing and are limited by the availability of time and expertise, resulting in smaller numbers of patients being screened for frailty.

There are some limitations to our study. First, only patients who were admitted with the relevant ICD-10 codes were included in the study; therefore, patients without any admissions were excluded from analysis. Secondly, as with studies using administrative data from electronic health records, the accuracy of ICD-10 codes can be inconsistent due to the complexity of medical terminology, leading to potential misclassification and incomplete data. To mitigate this, coders in our hospitals undergo structured training and admission codes are audited at regular intervals. Lastly, due to the retrospective design of our study, there was incomplete clinical data to calculate other liver prognostic scores such as Child Pugh score. However, the aim of this study was to identify on a broad level, cirrhosis patients at risk for frailty and complications, not to compare between liver prognostic scores.

In conclusion, we have shown that the HFRS can be used in a multi-ethnic Asian cirrhosis cohort in Singapore. More importantly, given that higher HFRS scores are correlated with increased mortality and complications such as readmissions, future studies can design and study interventions that might be able to prevent some of these complications. Many frailty-related interventions such as physical therapy and nutrition may alter the natural history of these patients. Frailty does not impact just older adults or those with chronic disease. It puts a greater demand and strain on existing healthcare system infrastructure, affecting resource utilization, not to mention the emotional and financial burdens on families and caregivers. Therefore, we propose that a frailty assessment serve as a necessary vital sign to properly inform clinical service provision and resource allocation. Using the HFRS can be a useful and cost-effective tool that can be calculated using administrative data to identify at-risk patients with cirrhosis to help improve health care delivery.

References

1. Elsheikh M, El Sabagh A, Mohamed IB, Bhongade M, Hassan MM, Jalal PK. Frailty in end-stage liver disease: Understanding pathophysiology, tools for assessment, and strategies for management. World J Gastroenterol. 2023;29(46):6028-48.
2. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. The Lancet. 2013;381(9868):752-62.
3. Lai JC, Tandon P, Bernal W, Tapper EB, Ekong U, Dasarathy S, Carey EJ. Malnutrition, Frailty, and Sarcopenia in Patients With Cirrhosis: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;74(3):1611-44.

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4. Chen HW, Dunn MA. Muscle at Risk: The Multiple Impacts of Ammonia on Sarcopenia and Frailty in Cirrhosis. Clinical and translational gastroenterology. 2016;7(5):e170.
5. Lai JC, Rahimi RS, Verna EC, Kappus MR, Dunn MA, McAdams-DeMarco M, Haugen CE, Volk ML, Duarte-Rojo A, Ganger DR, O'Leary JG, Dodge JL, Ladner D, Segev DL. Frailty Associated With Waitlist Mortality Independent of Ascites and Hepatic Encephalopathy in a Multicenter Study. Gastroenterology. 2019;156(6):1675-82.
6. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults: evidence for a phenotype. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(3):M146-56.
7. Lai JC, Covinsky KE, Dodge JL, Boscardin WJ, Segev DL, Roberts JP, Feng S. Development of a novel frailty index to predict mortality in patients with end-stage liver disease. Hepatology. 2017;66(2):564-74.
8. Tandon P, Tangri N, Thomas L, Zenith L, Shaikh T, Carbonneau M, Ma M, Bailey RJ, Jayakumar S, Burak KW, Abraldes JG, Brisebois A, Ferguson T, Majumdar SR. A Rapid Bedside Screen to Predict Unplanned Hospitalization and Death in Outpatients With Cirrhosis: A Prospective Evaluation of the Clinical Frailty Scale. Official journal of the American College of Gastroenterology | ACG. 2016;111(12):1759-67.
9. Hao B, Chen T, Qin J, Meng W, Bai W, Zhao L, Ou X, Liu H, Xu W. A comparison of three approaches to measuring frailty to determine adverse health outcomes in critically ill patients. Age and Ageing. 2023;52(6).
10. Eckart A, Hauser SI, Haubitz S, Struja T, Kutz A, Koch D, Neeser O, Meier MA, Mueller B, Schuetz P. Validation of the hospital frailty risk score in a tertiary care hospital in Switzerland: results of a prospective, observational study. BMJ Open. 2019;9(1):e026923.
11. Kilkenny MF, Phan HT, Lindley RI, Kim J, Lopez D, Dalli LL, Grimley R, Sundararajan V, Thrift AG, Andrew NE, Donnan GA, Cadilhac DA, Anderson C, Bernhardt J, Bew P, Bladin C, Cadigan G, Castley H, Lee A, Mackay M, Martyn S, McNeil J, Middleton S, Pollack M, Simcocks M, Simmonds F, Dewey H, Faux S, Hill K, Levi C, Price C, Bambery P, Bates T, Beltrame C, Blacker D, Butler E, Butler S, Crompton D, Crosby V, De Wytt C, Douglas D, Dunlop M, Easton P, Ermel S, Gange N, Geraghty R, Gill M, Hall G, Hand P, Herkes G, Hines K, Hishon F, Hughes J, Iedema J, Jude M, Kraemer T, Laird P, Madden J, Mahaffey G, Milosevic S, O'Brien P, Read S, Rowe K, Ryan F, Sabet A, Saines N, Salud E, Siller A, Staples C, White R, Wong A, Armstrong R, Churilov L, Dias A, Gibbs A, Grabsch B, Kung F, Lim J, Moss K, Paice K, Salama E, Small S, Stojanovic R, Street S, Tod E, Wallis K. Utility of the Hospital Frailty Risk Score Derived From Administrative Data and the Association With Stroke Outcomes. Stroke. 2021;52(9):2874-81.
12. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, Arora S, Street A, Parker S, Roberts HC, Bardsley M, Conroy S. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. The Lancet. 2018;391(10132):1775-82.
13. Kundi H, Wadhera RK, Strom JB, Valsdottir LR, Shen C, Kazi DS, Yeh RW. Association of Frailty With 30-Day Outcomes for Acute Myocardial Infarction, Heart Failure, and Pneumonia Among Elderly Adults. JAMA cardiology. 2019;4(11):1084-91.
14. Shah S, Goldberg DS, Kaplan DE, Sundaram V, Taddei TH, Mahmud N. Patient Frailty Is Independently Associated With the Risk of Hospitalization for Acute-on-Chronic Liver Failure. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2021;27(1):16-26.
15. Mahmud N, Kaplan DE, Taddei TH, Goldberg DS. Frailty Is a Risk Factor for Postoperative Mortality in Patients With Cirrhosis Undergoing Diverse Major Surgeries. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society. 2021;27(5):699-710.

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