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STUDY ON THE VALUE OF SERUM CYSTATIN C IN THE DIAGNOSIS OF ACUTE KIDNEY INJURY AND MORTALITY PROGNOSIS IN PATIENTS WITH DECOMPENSATED CIRRHOSIS

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The thesis can be found in:

- National Library of Vietnam
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INTRODUCTION

1. The necesssity of the research

Cirrhosis represents the final stage of chronic liver disease and remains a major health concern in both Vietnam and worldwide, with high rates of hospitalization and mortality, particularly when the disease progresses to the decompensated stage. At this stage, patients frequently develop severe complications such as ascites, gastrointestinal bleeding, hepatic encephalopathy, and infections. Among these, acute kidney injury (AKI) is a particularly serious complication, leading to prolonged hospitalization, increased healthcare costs, and higher mortality rates.

Early detection of acute kidney injury plays a crucial role in improving patient prognosis. However, serum creatinine-the biomarker most commonly used to assess renal function-often underestimates the degree of renal impairment in patients with cirrhosis due to reduced muscle mass and malnutrition, resulting in delayed diagnosis. Cystatin C, a biomarker less influenced by non-renal factors, has been shown to detect acute kidney injury earlier than creatinine and is closely associated with poor clinical outcomes; however, domestic research data on this marker remain limited.

These practical and scientific considerations provided the basis for conducting the present study entitled: **"*Study on the value of serum cystatin C in the diagnosis of acute kidney injury and mortality prognosis in patients with decompensated cirrhosis*"** with the following two objectives: **(**1). To determine serum cystatin C levels and their associations with selected clinical and laboratory characteristics in patients with decompensated cirrhosis. (2). To

evaluate the value of serum cystatin C levels in diagnosing acute kidney injury and predicting all-cause mortality in patients with decompensated cirrhosis.

2. Contributions of the thesis

This study further confirms the role of cystatin C in the early detection of renal dysfunction and in predicting mortality among patients with decompensated cirrhosis, thereby supporting risk stratification and guiding early clinical interventions in practice

3. Structure of the thesis

The thesis consists of 125 pages organized into four chapters, including 34 tables, 7 figures, 4 diagrams, and 14 charts. The reference list comprises 164 citations (12 in Vietnamese and 152 in English). The sections include: Introduction (4 pages), literature review (34 pages), materials and methods (27 pages), results (29 pages), discussion (27 pages), conclusions (2 pages), and recommendations (1 page).

Chapter 1. LITERATURE REVIEW

1.1. Overview of cirrhosis

Cirrhosis is the end stage of chronic liver disease, characterized by diffuse fibrosis and architectural distortion of the liver, leading to progressive hepatic dysfunction. Decompensated cirrhosis is marked by complications such as ascites, portal hypertension–related gastrointestinal bleeding, hepatic encephalopathy, or severe jaundice, and is associated with a substantially poorer prognosis than the compensated stage. In clinical practice, the Child–Pugh and MELD-Na scores are widely used to assess severity and predict outcomes; however, they do not fully

capture the impact of extrahepatic complications, particularly acute kidney injury (AKI).

1.2. Acute kidney injury in patients with cirrhosis

AKI is a frequent and severe complication in decompensated cirrhosis, with a prevalence of 20–50% and a markedly increased mortality risk. Although hepatorenal syndrome was previously regarded as the main cause of renal failure in cirrhosis, AKI is now defined based on dynamic changes in serum creatinine according to KDIGO and cirrhosis-specific updates. Renal function assessment is essential for monitoring and prognosis. However, serum creatinine may overestimate GFR in cirrhotic patients due to reduced muscle mass and fluid overload, while direct GFR measurement is not routinely feasible. Therefore, reliable biomarkers enabling earlier and more accurate renal assessment are needed.

1.3. Overview of serum cystatin C

Cystatin C is a low–molecular-weight protein (~13 kDa) that is freely filtered by the glomeruli and minimally affected by age, sex, or muscle mass, providing a more accurate estimate of GFR than creatinine, particularly in decompensated cirrhosis.

Studies have demonstrated its value in early AKI detection, identification of hepatorenal syndrome, and mortality prediction, even when creatinine remains normal. Prognostic models incorporating cystatin C have shown improved performance over traditional scores. However, findings remain inconsistent, and data from Vietnam are limited. Therefore, further evaluation of cystatin C in diagnosing AKI and predicting outcomes in decompensated cirrhosis is warranted.

Chapter 2. SUBJECTS AND METHODS OF RESEARCH

2.1. Research subjects

Patients with decompensated cirrhosis treated at the Department of Gastroenterology, Da Nang Hospital, from October 2022 to July 2025 were included in the study, with outcomes followed up until August 1, 2025. All laboratory tests were performed at the hospital's laboratory department under standardized quality control procedures.

2.1.1. Inclusion criteria

Age ≥18 years; diagnosis of decompensated cirrhosis; hospitalization during the study period; and provision of informed consent to participate in the study.

2.1.2. Exclusion criteria

Patients with conditions or receiving medications that may affect serum cystatin C or creatinine levels (such as thyroid dysfunction, corticosteroid therapy, or drugs influencing creatinine levels), those with structural kidney disease detected on ultrasonography, or those who declined participation in the study were excluded.

2.2. Diagnostic criteria and definitions

Decompensated cirrhosis: Defined as cirrhosis presenting with at least one decompensating event, including ascites, portal hypertension–related gastrointestinal bleeding, hepatic encephalopathy, or severe jaundice.

Acute kidney injury (AKI): In this study, acute kidney injury (AKI) was defined according to the KDIGO–ICA criteria. It was defined as an increase in serum creatinine ≥0.3 mg/dL within 48 hours or ≥1.5 times baseline within 7 days. Baseline creatinine was

obtained from pre-admission records when available; otherwise, the admission value was used. Creatinine was measured at admission, within 48 hours, and within 7 days. Urine output criteria were not applied. AKI staging followed KDIGO guidelines.

2.3. Study methods

The study used a cross-sectional descriptive design with prospective follow-up and no intervention. Sample size was calculated based on objectives related to AKI diagnosis and mortality prediction, with the larger required sample selected. A total of 161 eligible patients were consecutively enrolled during the study period to enhance reliability and minimize loss to follow-up.

2.4. Variables and data collection

Baseline variables, including age, sex, comorbidities, etiology of cirrhosis, and medication history, were collected, along with clinical characteristics and cirrhosis-related complications. Hematological, biochemical, and coagulation parameters, as well as prognostic scores including Child–Pugh, MELD, and MELD-Na, were recorded according to standard hospital procedures.

2.5. Laboratory methods and estimation of GFR

Serum creatinine levels were measured using the Cobas pro system (Roche). Serum cystatin C was quantified at hospital admission using the particle-enhanced turbidimetric immunoassay (PETIA) method. Estimated glomerular filtration rate (eGFR) was calculated using CKD-EPI equations based on creatinine, cystatin C, or a combination of both biomarkers.

2.6. Study procedures and follow-up

After informed consent, clinical and laboratory data were collected. Survival was assessed at 30 days and at 3, 6, and 12

months. Unreachable patients were considered lost to follow-up.

2.7. Statistical analysis

Data were analyzed using Microsoft Excel and SPSS 26.0. Group comparisons, correlation, and regression analyses were performed as appropriate. Diagnostic accuracy was assessed by ROC curves and AUC, and survival was analyzed using the Kaplan–Meier method. A p-value < 0.05 was considered statistically significant.

2.8. Research ethics

The study was approved by the Ethics Committee of Hue University of Medicine and Pharmacy, Hue University, and was authorized for implementation at Da Nang Hospital.

Chapter 3. RESULTS

3.1. General characteristics of the study population

Total of 161 patients with decompensated cirrhosis treated at Da Nang Hospital were enrolled in the study. The mean age was 58.2 ± 12.6 years, and the majority of patients were male (76.4%).

3.2. Cystatin C and their associations with clinical and laboratory characteristics in decompensated cirrhosis patients.

3.2.1. Characteristics of cystatin C levels in the study population

Table 3.1. Cystatin C levels at hospital admission

Cystatin C(mg/L)	**(n=161)**	**%**
Elevated (>1.02)	96	59,6
Not elevated	65	40,4
Mean ± SD	1,29 ± 0,60	
Median (interquartile range)	1,09 (0,95 - 1,39)	

Comment: The mean serum cystatin C level was 1.29 ± 0.60 mg/L, with 59.6% of patients showing elevated cystatin C levels.

3.2.2. Association between serum cystatin C and related factors in patients with decompensated cirrhosis

Table 3.2. Univariate linear regression analysis of factors associated with serum cystatin C in patients with decompensated cirrhosis

Variable	B	r	p	95% CI B	
				Lower	Upper
History of diuretic use	0,443	0,234	**0,003**	0,155	0,731
History of NSAID use	0,017	0,009	0,909	-2,73	0,306
History of ACE inhibitor use	-0,167	-0,079	0,319	-0,497	0,163
Age	0,006	0,127	0,109	-0,001	0,014
Female sex	0,018	0,013	0,873	-0,202	0,238
Ascites	0,272	0,227	**0,004**	0,089	0,455
Gastrointestinal bleeding	0,268	0,206	**0,009**	0,468	0,069

Comment: Cystatin C levels were significantly associated with diuretic use, ascites, and gastrointestinal bleeding.

3.2.3. Correlation between serum cystatin C and estimated GFR using the CKD-EPI 2021 creatinine–cystatin C equation

Table 3.3. Correlation between serum cystatin C and estimated GFR calculated using the CKD-EPI 2021 creatinine–cystatin C equation

Parameter	Cystatin C		Creatinin	
	r	p	**r**	p
CKD-EPI 2021 (creatinine–cystatin C)	-0,780	**<0,001**	-0,640	**<0,001**

Comment: Serum cystatin C showed a stronger inverse correlation with eGFR calculated using the CKD-EPI 2021 creatinine–cystatin C equation compared with serum creatinine ($r = -0.780$ vs. $r = -0.640$; $p < 0.001$).

3.2.4. Correlation between serum cystatin C levels and prognostic scores in patients with decompensated cirrhosis

Table 3.4. Association between serum cystatin C and Child–Pugh classification, MELD, and MELD-Na scores

Cystatin C / Scoring system		Elevated		Not elevated		p	Median (IQR)	p
		n	%	n	%			
Child-Pugh	C	54	69,2	24	30,8	**0,016**	1,28	**0,001**
	A+B	42	50,6	41	49,4		1,03	
MELD	≥ 11	76	60,3	50	39,7	0,735	1,11	0,351
	< 11	20	57,1	15	42,9		1,04	
MELD-Na	≥ 30	25	83,3	5	16,7	**0,003**	1,43	**<0,001**
	< 30	71	54,2	60	45,8		1,04	

Comment: Nồng độ cystatin C huyết thanh tăng có liên quan có ý nghĩa thống kê với mức độ nặng của xơ gan, ghi nhận tỷ lệ cao hơn ở nhóm Child–Pugh C so với Child–Pugh A và B (p = 0,016), và ở nhóm có điểm MELD-Na ≥30 so với <30 (p = 0,003).

Table 3.5. Correlation between serum cystatin C levels and prognostic scores in patients with decompensated cirrhosis

Parameter	Cystatin C		Creatinin	
	r	p	**r**	p
Child-Pugh	0,340	**<0,001**	0,251	**0,001**
MELD	0,409	**<0,001**	0,437	**<0,001**
MELD-Na	0,389	**<0,001**	0,296	**<0,001**

Comment: Both biomarkers correlated moderately with prognostic scores; however, cystatin C showed stronger associations with Child–Pugh and MELD-Na.

3.3. Value of serum cystatin C in the diagnosis of acute kidney injury in patients with decompensated cirrhosis

3.3.1. Characteristics of acute kidney injury in patients with decompensated cirrhosis

Table 3.6. Prevalence and staging of acute kidney injury

Parameter	n	%
Acute kidney injury (AKI)		
Present	50	31,1
Absent	111	68,9
AKI stage		
Stage 1	27	54,0
Stage 2	13	26,0
Stage 3	10	20,0

Comment: Acute kidney injury was observed in 31.1% of patients, with the majority classified as stage 1, a considerable proportion of cases were also identified in stages 2 and 3.

3.3.2. Diagnostic value of serum cystatin C in acute kidney injury among patients with decompensated cirrhosis

Table 3.7. Prevalence of elevated cystatin C in patients with AKI

Creatinin	(n=50)	%	Cystatin C	(n=50)	%
Elevated	17	34,0	Elevated	15	88,2
			Not elevated	2	11,8
Không tăng	**33**	66,0	Elevated	**25**	**75,8**
			Not elevated	8	24,2

Comment: Among patients with acute kidney injury, 75.8% of cases without elevated serum creatinine already showed elevated cystatin C levels at hospital admission.

Table 3.8. Univariate and multivariate binary logistic regression analysis of factors associated with acute kidney injury

Variable	Univariate analysis		Multivariate analysis	
	OR	p	OR (95% CI)	p
History of diuretic use	7,45	**<0,001**	4,58	**0,020**
Serum cystatin C	9,08	**<0,001**	8,82	**0,001**
Admission serum creatinine	1,01	**0,013**	0,99	0,293
Child-Pugh score	1,29	**0,003**	0,92	0,633
MELD Na score	1,05	**0,003**	1,00	0,894
INR	2,38	**0,017**	1,79	0,331
Albumin(g/L)	0,93	**0,016**	0,96	0,339
Ure (mmol/L)	1,14	**0,002**	1,12	0,063
Total bilirubin (µmol /L)	1,00	**0,004**	1,00	0,481

Comment: In multivariate analysis, only a history of diuretic use and serum cystatin C levels remained independently associated with acute kidney injury, whereas the other variables were no longer statistically significant after adjustment.

Table 3.9. Sensitivity, specificity, and AUC-ROC of serum cystatin C and other indicators for predicting acute kidney injury

Indicator	**Acute kidney injury (AKI)**				
	Cut-off value	**Sensitivity (%)**	**Specificity (%)**	**AUC ROC 95% CI**	**p**
Cystatin C	>1,38	56,0	89,2	0,762	**<0,001**
Child-Pugh	>10	44,0	77,5	0,644	**0,002**
BUN	>7,2	52,0	81,1	0,631	**0,010**
Creatinin	>91	44,0	88,3	0,574	0,206
MELD	>17,1	60,0	73,0	0,644	**0,004**
MELD-Na	>21,3	66,0	64,9	0,652	**0,004**

Comment: Serum cystatin C demonstrated the best diagnostic performance for acute kidney injury (AUC = 0.762; p < 0.001),

whereas the other indicators showed only moderate performance, and serum creatinine did not reach statistical significance.

3.4. Prognostic value of serum cystatin C for mortality in patients with decompensated cirrhosis

3.4.1. Mortality characteristics in patients with decompensated cirrhosis

Table 3.10. Mortality outcomes in the study population

Cumulative mortality		**Number (n)**	**Percentage (%)**
Survived		**128**	**79,5**
Died	Within 30 days	10	6,2
	Within 3 months	25	15,5
	Within 6 months	28	17,4
	Within 12 months	33	20,5

Comment: The cumulative mortality rates were 6.2% at 30 days, 15.5% at 3 months, 17.4% at 6 months, and 20.5% at 12 months of follow-up.

3.4.2. Prognostic value of serum cystatin C for 30-day mortality in patients with decompensated cirrhosis

Table 3.11. Univariate and multivariate Cox regression analyses of factors associated with 30-day mortality

Variables	**Univariate analysis**		**Multivariate analysis**	
	HR	p	HR (95% CI)	p
Cystatin C	2,66	**<0,001**	2,93	**<0,001**
Creatinine at admission	1,02	**<0,001**	1,00	0,492
MELD-Na	1,11	**<0,001**	1,12	**0,007**
Child-Pugh	1,39	**0,033**	0,69	0,097

Comment: Multivariate analysis, only cystatin C and MELD-Na remained independent predictors of 30-day mortality, whereas

creatinin and the CP score were no longer statistically significant.

Table 3.12. Sensitivity, specificity, and AUC–ROC of serum cystatin C and selected variables in predicting 30-day mortality

Variables	Mortality				
	Cut-off value	**Sensitivity (%)**	**Specificity (%)**	**AUC ROC (95%CI)**	**p**
Cystatin C	>1,49	80,0	85,4	0,851	**<0,001**
Creatinin	>94,9	50,0	81,5	0,576	0,530
MEDL Na	>29,1	80,0	83,4	0,797	**0,002**
Child-Pugh	>9	70,0	53,0	0,664	0,071

Comment: Serum cystatin C demonstrated the highest predictive accuracy for 30-day mortality (AUC = 0.851), outperforming the MELD-Na score, whereas serum creatinine and the Child–Pugh score did not reach statistical significance.

3.4.3. Prognostic value of serum cystatin C for 3-month mortality in patients with decompensated cirrhosis

Table 3.13. Univariate and multivariate Cox regression analyses of factors associated with 3-month mortality

Variables	Univariate analysis		Multivariate analysis	
	HR	p	HR (95% CI)	p
Cystatin C	3,77	**<0,001**	3,331	**<0,001**
Creatinin at admission	1,01	**<0,001**	1,005	0,139
MELD-Na	1,07	**<0,001**	1,051	0,067
Child-Pugh	1,25	**0,016**	0,895	0,412

Comment: Multivariate analysis, only cystatin C remained an independent predictor of 3-month mortality, whereas other variables, were no longer statistically significant after adjustment.

Table 3.14. Sensitivity, specificity, and AUC–ROC of serum cystatin C and selected variables in predicting 3-month mortality

Variables	Mortality				
	Cut-off value	**Sensitivity (%)**	**Specificity (%)**	**AUC ROC (95%CI)**	**p**
Cystatin C	>1,49	76,0	91,9	0,835	**<0,001**
Creatinin	>76,5	68,0	71,3	0,716	**<0,001**
MELD-Na	>26,7	64,0	80,1	0,710	**0,002**
Child-Pugh	>10	48,0	73,5	0,625	0,063

Comment: Cystatin C demonstrated the best predictive performance for 3-month mortality (AUC = 0.835), outperforming creatinin, MELD-Na, the CP did not reach statistical significance.

3.4.4. Prognostic value of serum cystatin C for 6-month mortality in patients with decompensated cirrhosis

Table 3.15. Univariate and multivariate Cox regression analyses of factors associated with 6-month mortality

Variables	Univariate analysis		Multivariate analysis	
	HR	p	HR (95% CI)	p
Cystatin C	3,82	**<0,001**	3,33	**<0,001**
Creatinin at admission	1,01	**<0,001**	1,00	0,196
MELD-Na	1,07	**<0,001**	1,04	0,124
Child-Pugh	1,27	**0,008**	0,95	0,711

Comment: Multivariate analysis, only cystatin C remained an independent predictor of 6-month mortality, whereas the other variables were no longer statistically significant after adjustment.

Table 3.16. Sensitivity, specificity, and AUC–ROC of serum cystatin C and selected variables in predicting 6-month mortality

Variables	Mortality				
	Cut-off value	Sensitivity (%)	Specificity (%)	AUC ROC (95%CI)	p
Cystatin C	>1,37	78,6	85,7	0,843	**<0,001**
Creatinin	>76,5	64,3	71,4	0,689	**0,002**
MEDL Na	>26,7	60,7	80,5	0,702	**0,001**
Child-Pugh	>11	35,7	85,0	0,633	**0,032**

Comment: Cystatin C demonstrated the highest predictive value for 6-month mortality (AUC = 0.843), outperforming creatinin, MELD-Na, and Child–Pugh.

3.4.5. Prognostic value of serum cystatin C for 12-month mortality in patients with decompensated cirrhosis

Table 3.17. Univariate and multivariate Cox regression analyses of factors associated with 12-month mortality

Variables	Univariate analysis		Multivariate analysis	
	HR	p	HR (95% CI)	p
Cystatin C	3,64	**<0,001**	3.06	**<0,001**
Creatinine at admission	1,01	**<0,001**	1,00	0,285
MELD Na	1,06	**<0,001**	1,03	0,249
Child-Pugh	1,36	**<0,001**	1,04	0,722

Comment: Multivariate analysis, only cystatin C remained an independent predictor of 12-month mortality, whereas the remaining variables were no longer statistically significant after adjustment.

Table 3.18. Sensitivity, specificity, and AUC–ROC of cystatin C in predicting 12-month mortality

Variables	Mortality				
	Cut-off value	**Sensitivity (%)**	**Specificity (%)**	**AUC ROC (95% CI)**	**p**
Cystatin C	>1,49	60,6	92,2	0,769	**<0,001**
Creatinin	>85,5	48,5	80,5	0,639	**0,023**
MEDL Na	>26,7	51,5	79,7	0,681	**0,001**
Child-Pugh	>10	54,5	77,3	0,696	**0,011**

Comment: Cystatin C demonstrated the best predictive performance for 12-month mortality (AUC = 0.769), with high specificity, outperforming creatinin, MELD-Na, and Child–Pugh.

Chapter 4. DISCUSSION

4.1. Cystatin C and their association with selected clinical and laboratory characteristics in decompensated cirrhosis patients

4.1.1. Serum cystatin C levels in the study population

The mean serum cystatin C level in patients with decompensated cirrhosis was 1.29 ± 0.6 mg/L, with no significant variation by age or sex. This value is comparable to previous reports in decompensated cirrhosis, but lower than levels observed in patients with AKI or HRS.

4.1.2. Association cystatin C levels and clinical manifestations

Elevated serum cystatin C levels were significantly associated with severe decompensating manifestations, including diuretic use,

ascites, and gastrointestinal bleeding. These findings are consistent with the pathophysiological mechanism of reduced effective arterial blood volume, ultimately leading to a decline in glomerular filtration rate. This suggests that cystatin C not only reflects renal function but may also indirectly indicate the degree of hemodynamic disturbance, whereas serum creatinine may underestimate renal dysfunction due to reduced muscle mass. These results further support the role of cystatin C in assessing disease severity and stratifying the risk of early renal impairment in patients with decompensated cirrhosis.

4.1.3. Predictive value of serum cystatin C for reduced glomerular filtration rate in patients with cirrhosis

In this study, serum cystatin C showed a strong inverse correlation with eGFR calculated by the CKD-EPI 2021 equation ($r = -0.780$; $p < 0.001$), stronger than serum creatinine, and demonstrated high accuracy in predicting reduced GFR. These findings align with previous studies and meta-analyses indicating that cystatin C more reliably reflects GFR than creatinine, particularly in patients with ascites. Overall, cystatin C is a valuable biomarker for early detection of renal dysfunction and risk stratification in decompensated cirrhosis.

4.1.4. Association between serum cystatin C levels and prognostic scoring systems in patients with cirrhosis

Elevated serum cystatin C levels were closely associated with more severe hepatic decompensation, particularly in patients with Child–Pugh C and MELD-Na ≥ 30, reflecting the link between advanced liver failure and renal dysfunction. Cystatin C showed moderate positive correlations with Child–Pugh, MELD, and MELD-Na scores, indicating that it reflects not only renal function

but also overall disease severity and hemodynamic impairment. These findings are consistent with previous studies and support the role of cystatin C in severity assessment and risk stratification in decompensated cirrhosis.

4.2. Diagnostic value of serum cystatin C in acute kidney injury among patients with decompensated cirrhosis

4.2.1. Incidence and staging of AKI in the study population

The present study applied the KDIGO–ICA criteria, with serum creatinine monitored at admission, within 48 hours, and over the first 7 days. In cases where baseline creatinine was unavailable, it was estimated to minimize underdiagnosis of acute kidney injury (AKI). The incidence of AKI was 31.1%, comparable to several domestic studies but lower than reports involving more critically ill populations.These differences are primarily attributable to variations in diagnostic criteria, disease severity, and the frequency of creatinine monitoring. Additionally, the high prevalence of infection in this cohort likely contributed to an increased risk of AKI. Regarding staging, AKI stage 1 predominated (54.0%), followed by stages 2 and 3, consistent with the general trend observed in studies not specifically focused on critically ill or intensive care populations.

4.2.2. Diagnostic value of serum cystatin C in acute kidney injury among patients with decompensated cirrhosis

Serum cystatin C levels were significantly higher in the AKI group, whereas serum creatinine showed no significant difference. This supports evidence that cystatin C may rise even when creatinine remains normal, particularly in advanced cirrhosis or hepatorenal syndrome. Multivariate analysis identified cystatin C as the strongest independent predictor of AKI, with diuretic use also independently

associated. ROC analysis demonstrated superior diagnostic performance of cystatin C over creatinine (cut-off >1.38 mg/L, high specificity). Notably, many patients had elevated cystatin C despite normal creatinine at admission, indicating potential underdiagnosis if relying solely on creatinine. Early measurement of cystatin C may therefore improve timely AKI detection and risk stratification in decompensated cirrhosis.

4.3. Prognostic value of serum cystatin C for mortality in patients with decompensated cirrhosis

4.3.1. Association serum cystatin C and 30-day mortality

4.3.1.1. Thirty-day mortality in the study population

The 30-day mortality rate was 6.2%, which is lower than that reported in studies involving more critically ill or intensive care unit populations, yet remains consistent with outcomes observed in routine clinical practice. This difference is primarily attributable to the characteristics of the study population, underscoring the continued importance of early prognostic assessment using biomarkers such as serum cystatin C.

4.3.1.2. Association serum cystatin C and 30-day mortality

Cox regression analysis demonstrated that serum cystatin C was the strongest independent predictor of 30-day mortality, whereas serum creatinine and the Child–Pugh score were no longer statistically significant after adjustment. Receiver operating characteristic (ROC) analysis further confirmed the superior discriminative ability of cystatin C for short-term mortality (AUC = 0.851), exceeding that of serum creatinine, MELD-Na, and Child–Pugh scores. These findings are consistent with international studies by Hong C., Leem A.Y., and Nagy E., in which cystatin C was identified as an independent predictor of short-term mortality.

4.3.2. Association serum cystatin C and 3-month mortality

4.3.2.1. Three-month mortality in the study population

The 3-month mortality rate was 15.5%, comparable to that reported in cohorts with similar disease severity, whereas studies involving more critically ill or intensive care unit populations have generally documented higher rates. These findings suggest that the study results reasonably reflect routine clinical practice and are therefore appropriate for evaluating the prognostic value of serum cystatin C in a broader patient population.

4.3.2.2. Association serum cystatin C and 3-month mortality

Serum cystatin C levels were significantly higher in the mortality group, reflecting underlying renal dysfunction and systemic decompensation. Cox regression identified cystatin C as the strongest independent predictor of 3-month mortality, while serum creatinine and liver scores lost significance after adjustment. ROC analysis confirmed superior discriminatory performance of cystatin C (optimal cut-off >1.49 mg/L), consistent with international studies recognizing its independent prognostic value for intermediate-term mortality in cirrhosis.

4.3.3. Association serum cystatin C and 6-month mortality

4.3.3.1. Six-month mortality in the study population

The 6-month mortality rate was 17.4%, comparable to that reported in cohorts with a similar degree of hepatic decompensation, such as those described by Kim T.H. and Seo Y.S. In contrast, studies involving patients with more severe complications—particularly those complicated by acute kidney injury (AKI)—have documented substantially higher mortality rates, underscoring the critical role of renal complications in determining intermediate-term prognosis among patients with decompensated cirrhosis.

4.3.3.2. Association serum cystatin C and 6-month mortality

Serum cystatin C was strongly associated with 6-month mortality and remained an independent prognostic factor in

multivariate analysis, whereas serum creatinine and Child–Pugh score lost statistical significance. ROC analysis confirmed its superior predictive performance compared with traditional indices. These findings are consistent with previous international studies, supporting the role of cystatin C in intermediate-term mortality risk stratification in patients with decompensated cirrhosis.

4.3.4. Association serum cystatin C and 12-month mortality

4.3.4.1. Twelve-month mortality in the study population

The 12-month mortality rate was 20.5%, comparable to that reported in cohorts with a similar degree of hepatic decompensation, such as those described by Kim T.H. and Seo Y.S. In contrast, studies involving more severely ill patients—particularly those complicated by acute kidney injury (AKI)—have documented substantially higher mortality rates, further emphasizing the critical role of renal complications in determining long-term prognosis in patients with decompensated cirrhosis.

4.3.4.2. Association serum cystatin C and 12-month mortality

Serum cystatin C emerged as the strongest independent predictor of 12-month mortality, whereas serum creatinine and conventional liver scoring systems lost statistical significance after adjustment. Receiver operating characteristic (ROC) analysis further demonstrated that cystatin C exhibited superior discriminatory performance for mortality compared with serum creatinine, Child–Pugh, and MELD-Na scores. These findings are consistent with several international studies, including those by Kim T.H, Seo Y.S, Teneva B.H, and Mauro E.

CONCLUSION

Based on 161 patients with decompensated cirrhosis treated at Da Nang Hospital, the following conclusions were drawn:

1. Serum cystatin C levels and their association with clinical and laboratory characteristics.

The mean serum cystatin C level was 1.29 ± 0.60 mg/L and was not influenced by age or sex. However, levels were significantly higher in patients with decompensating features such as ascites, gastrointestinal bleeding, and diuretic use.

Cystatin C showed a strong inverse correlation with eGFR calculated by the CKD-EPI 2021 equation ($r = -0.777$; $p < 0.001$), stronger than that of serum creatinine, and demonstrated moderate positive correlations with Child–Pugh, MELD, and MELD-Na.

2. Diagnostic and prognostic value of serum cystatin C

2.1. Diagnostic value in acute kidney injury

The incidence of AKI according to ICA–KDIGO criteria was 31.1%, predominantly stage 1. Serum cystatin C levels were significantly higher in patients with AKI. Multivariate analysis identified cystatin C and prior diuretic use as independent risk factors, whereas serum creatinine was not significant.

Cystatin C showed good diagnostic accuracy (AUC = 0.762); at a cut-off ≥1.38 mg/L, it provided high specificity, supporting early detection of AKI.

2.2. Prognostic value for mortality

Cystatin C independently predicted mortality at 30 days, 3, 6, and 12 months. It consistently outperformed creatinine and enhanced risk stratification when integrated with liver prognostic scores.

- 30-day mortality: 6.2%; cystatin C was an independent predictor (HR = 2.93; $p < 0.001$), with AUC = 0.851 at a cut-off

>1.49 mg/L.

- 3-month mortality: 15.5%; cystatin C remained independently associated with mortality (HR = 3,331; p < 0.001), with AUC = 0.835 and high specificity.

- 6-month mortality: 17.4%; cystatin C maintained independent prognostic value (HR = 3.33; p < 0.001), with AUC = 0.843.

- 12-month mortality: 20.5%; cystatin C continued to be an independent predictor (HR = 3.06; p < 0.001), with AUC = 0.769 and high specificity.

PUBLICATIONS OF RESEARCH RESULTS OF THE THESIS

1. Nguyen Thanh Trung, Tran Xuan Chuong (2025). *"Evaluation of the value of serum cystatin C in estimating glomerular filtration rate in patients with cirrhosis treated at Da Nang Hospital."* Hue Journal of Medicine and Pharmacy, No. 5, Vol. 15, 2025.

2. Nguyen Thanh Trung, Tran Xuan Chuong (2025). *"Association between serum cystatin C levels and Child–Pugh classification, MELD, and MELD-Na scores in patients with decompensated cirrhosis at Da Nang Hospital."* Journal of Clinical Medicine – Hue Central Hospital, Vol. 17, No. 7, 2025.

3. Nguyen Thanh Trung, Tran Xuan Chuong (2025). *"Diagnostic value of serum cystatin C in predicting acute kidney injury and 90-day mortality in patients with decompensated cirrhosis treated at Da Nang Hospital."* Vietnam Medical Journal, Vol. 554, September 2025, Issue 2.