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Hemoglobin Glycation Index (HGI) and in-hospital prognosis in patients with Acute Decompensated Heart Failure

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ABSTRACT

Background: ADHF usually induces in-hospital hyperglycemia which initiates cardiac glucotoxicity. HGI is considered a simple marker to diagnose in-hospital hyperglycemia and its prognostic impact in patients hospitalized with ADHF.

Aim of study: This study aimed to assess the ability of HGI to predict in-hospital mortality and other adverse clinical outcome and in hospitalized patients with ADHF.

Methods: The participants were all hospitalized patients with rapid development of exaggerated symptoms and signs of congestion due to heart failure (HF) that confirmed by presence of elevated brain natriuretic peptide hormone (BNP) levels and evidence of structural heart disease diagnosed transthoracic echocardiography at time of hospital admission. HGI is the difference between the measured hemoglobin A1c (HbA1c) and the predicted HbA1c obtained by this equation (predicted HbA1c = 0.024 FPG + 3.1).

Results: the values of HGI above (2.54%) had a sensitivity of 68.4% and specificity of 87.6% (AUC=0.821, P value<0.001) to predict in-hospital mortality and the values of HGI above (1.28%) had a sensitivity of 87.2% and specificity of 78.2% (AUC=0.860, P value<0.001) to predict other in-hospital adverse clinical outcome among patients who were admitted with ADHF during their hospital course.

Conclusion: HGI is considered as independent marker for the risk of in-hospital mortality and other adverse clinical outcomes in the patients hospitalized with ADHF.

KEYWORDS: Hemoglobin Glycation Index (HGI), Acute Decompensated Heart Failure, In-Hospital Mortality; Adverse Clinical Outcomes; Hyperglycemia.

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INTRODUCTION

Acute decompensated heart failure (ADHF), represents one of the leading causes of hospitalizations in Europe and the United States, especially in the subpopulation of patients with advanced age [1]. Furthermore, mortality in ADHF remains high with in-hospital mortality rates ranging from 5% to 8% and one year mortality rates from 20–30% as being observed in contemporary registries [2]. ADHF defined as gradual or rapid worsening of heart failure (HF) signs and symptoms (e.g. dyspnea, fluid retention, or fatigue) that needs urgent hospitalization and intravenous medications. It may occur as the first manifestation of HF or as a complication during the native course of HF [3]. ADHF can induce in-hospital hyperglycemia which stimulates cardiac glucotoxicity as a result to mitochondrial impairment, oxidative stress-related cell injury and endothelial damage [4]. The hemoglobin glycation index (HGI) is considered as simple marker to diagnose in-hospital hyperglycemia and its prognostic impact in patients hospitalized with ADHF [5]. HGI is the difference between the individual's observed hemoglobin A1c (HbA1c) and a predicted HbA1c obtained by inserting fasting blood glucose measurement in this equation (predicted HbA1c = 0.024 FPG + 3.1) [6]. Our study emphasized on the prognostic role of HGI to predict in-hospital mortality and adverse outcome in hospitalized patients with ADHF, and comparing the in-hospital mortality with the Get with the Guidelines–Heart Failure (GWTG-HF) risk score in these patients [7].

PATIENTS AND METHODS

The established study was a prospective cohort study aimed to assess the ability of HGI to predict in-hospital adverse clinical outcome and mortality in hospitalized patients with ADHF and compare between HGI and GWTG-HF risk score that estimated at the time of hospital admission for prediction of mortality in these patients. ADHF was defined as clinical presentation with exaggerated symptoms and signs of congestion due to heart failure (HF) requiring urgent hospitalization and usually intravenous therapy [3].

Inclusion criteria: All enrolled patients in the study were ≥ 18 years of age who emergently hospitalized at Capital University Badr hospital with rapid development of exaggerated symptoms and signs of congestion due to heart failure (HF) that confirmed by presence of elevated brain natriuretic peptide hormone (BNP) levels and evidence of structural

heart disease diagnosed by standardized transthoracic echocardiography at time of hospital admission according to the '2021 European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic HF [8]. All echocardiographic studies were interpretated by two independent cardiologists blinded to the final data analysis.

Exclusion criteria: Patients presented with two or more SIRS criteria of sepsis, cardiogenic shock, end stage renal disease on regular hemodialysis, liver cell failure, active myocardial ischemia and signs of organ hypoperfusion were excluded from the study to prevent negatively impacting the statistical results of the patients' prognosis **(Figure 1).**

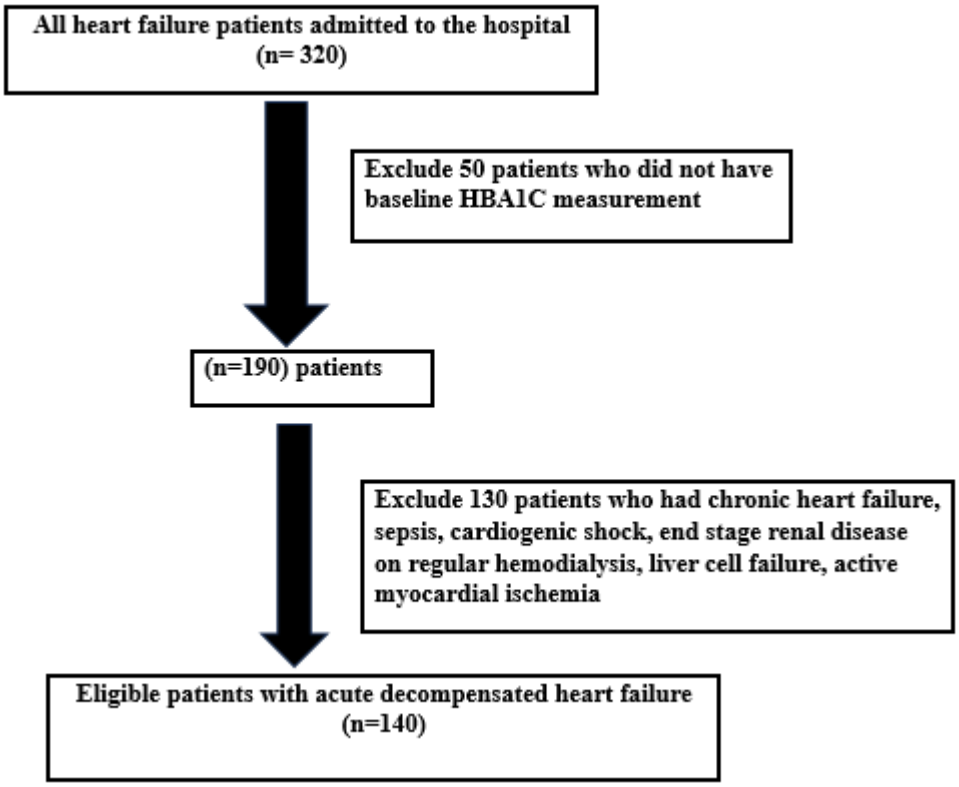

Figure 1. Flow chart of patients' inclusion and exclusion criteria

Study primary end points: The primary outcome was in-hospital all-cause mortality (defined as all-cause mortality during the index hospitalization), acute myocardial infarction (AMI), stroke, cardiogenic shock, acute kidney injury (AKI) and life-threatening arrhythmia.

Methodology: All participants in the study were undergone medical history taking, general and local cardiac examinations then blood sample was taken at the time of ICU admission for routine laboratory investigations., such as complete blood count, serum creatinine, blood urea, ALT, AST, serum albumin, serum potassium and HBA1c. Fasting blood glucose level (FBG) was measured after fasting for eight hours after ICU admission from another blood sample. HGI was calculated by subtracting the predicted value of HBA1c determined by FBG level from the measured value of HBA1c at time of ICU admission. Predicted HBA1c was derived from linear regression equation according to NHANES reference as (predicted HbA1c = 0.024 FPG + 3.1) [6]. Twelve leads resting ECG and echocardiography were also carried out for all study individuals. GWTG-HF risk score was estimated for every individual when primary admitted to ICU. GWTG-HF risk score is used to predict in-hospital mortality based on a cohort of 39,783 patients in 198 hospitals. Multivariable logistic regression identified the following seven predictors from the derivation samples; systolic blood pressure, age, blood urea, heart rate, sodium, chronic obstructive pulmonary disease and race [9]. GWTG-HF risk score values were correlated with HGI values for the ability to predict in-hospital mortality in patients hospitalized with ADHF.

Statistical analysis

Categorical variables are presented as frequencies and proportions and comparison between groups was done by Pearson chi-square or Fisher exact test. Continuous variables are presented as mean ± SD or medians (interquartile range) and comparison between was done using Student *t* tests or Mann-Whitney U test. The prognostic value of HGI for predicting adverse clinical outcomes was analyzed using the receiver-operating characteristic (ROC) curve, with a best cut-off value, sensitivity, specificity, areas under curve (AUC), 95% confidence intervals (CI), and p value. Multivariable logistical regression analysis was used to adjusted for variables that at univariable analysis had $P<0.05$ was considered statistically significant. The statistical analysis was done using SPSS version 22.0.

RESULTS

Table (1): Demographic and clinical characteristics of the studied patients

	Total 140
Age, years	60 [50-68]
Male sex	84 (60.0%)
BMI, kg/m^2	27.4 [26.3-29.7]
Active smoker	63 (45.0%)
Hypertension	70 (50.0%)
Diabetes mellitus	70 (50.0%)
Chronic kidney disease	42 (30.0%)
Ischemic heart disease	91 (65.0%)
Dyslipidemia	77 (55.0%)

One hundred and forty patients of ADHF were included in this prospective cohort study. The age of the study population ranged from 50 to 68 years and males represented 60% of them ***(Table 1).***

Table (2): Baseline characteristics and comparisons by in-hospital mortality and any adverse in-hospital outcome

	Alive (n=121)	Died (n=19)	**P-value**	Good outcome (n=101)	Poor outcome (n=39)	**P-value**
Age, years	60 [48-68]	62 [60-66]	**0.047**	60 [45-70]	60 [57-62]	0.387
Male sex	67 (55.4%)	17 (89.5%)	**0.005**	55 (54.5%)	29 (74.4%)	0.031
BMI, kg/m^2	27.3 [24.828.7]	33.0 [31.0-33.0]	**<0.001**	27.3 [24.6-27.6]	32.0 [27.6-33.0]	**<0.001**
Active smoker	48 (39.7%)	15 (78.9%)	**0.001**	40 (39.6%)	23 (59.0%)	**0.039**
Hypertension	59 (48.8%)	11 (57.9%)	0.459	48 (47.5%)	22 (56.4%)	0.346
Diabetes mellitus	54 (44.6%)	16 (84.2%)	**0.001**	35 (34.7%)	35 (89.7%)	**<0.001**
Chronic kidney disease	38 (31.4%)	4 (21.1%)	0.360	27 (26.7%)	15 (38.5%)	0.175
Ischemic heart disease	73 (60.3%)	18 (94.7%)	**0.003**	60 (59.4%)	31 (79.5%)	**0.026**
Dyslipidemia	60 (49.6%)	17 (89.5%)	**0.001**	45 (44.6%)	32 (82.1%)	**<0.001**
Fasting blood glucose, mg/dL	111 [98-130]	156 [132-156]	**<0.001**	105 [98-127]	140 [130-156]	**<0.001**
HbA1c, %	6.0 [5.8-7.5]	11.0 [7.6-11.0]	**<0.001**	6.0 [5.5-7.0]	9.0 [7.5-11.0]	**<0.001**
Serum creatinine, mg/dL	1.2 [0.9-2.5]	1.4 [1.1-1.4]	0.670	1.2 [0.9-1.8]	1.4 [1.2-2.5]	**<0.001**
Creatinine clearance, mL/min	88.0 [47.0-94.0]	85.0 [82.0-86.5]	0.432	88.0 [58.0-94.4]	82.0 [46.4-88.8]	**0.015**
Albumin, g/dL	3.3 [2.8-3.6]	2.4 [2.2-3.2]	**<0.001**	3.2 [2.8-3.6]	3.2 [2.3-3.3]	0.081
AST, U/L	59 [35-100]	66 [62-95]	0.297	59 [35-89]	95 [38-152]	**0.039**
ALT, U/L	42 [25-85]	54 [48-139]	**0.013**	42 [28-64]	85 [25-168]	**0.036**
Sodium, mmol/L	134 [129-140]	130 [129-134]	0.249	134 [129-139]	132 [129-142]	0.425
Potassium, mmol/L	4.2 [4.0-4.8]	4.3 [3.5-4.8]	0.184	4.2 [4.0-4.8]	4.8 [3.5-4.9]	0.720
Hemoglobin, g/dL	10.9 [10.0-12.4]	11.0 [10.6-13.0]	0.178	11.0 [10.0-13.0]	10.6 [10.0-11.8]	0.252
WBC, ×10^9/L	10.0 [8.0-12.3]	12.3 [9.0-13.2]	**0.025**	10.0 [8.0-12.3]	9.0 [8.0-13.0]	0.614
Platelets, ×10^9/L	266 [212-328]	366 [189-366]	0.154	266 [212-323]	311 [189-375]	0.262
SBP, mmHg	120 [110-140]	100 [90-105]	**<0.001**	120 [110-140]	100 [95-130]	**0.014**
DBP, mmHg	80 [70-90]	60 [60-70]	**<0.001**	80 [70-90]	60 [60-80]	**0.045**
MAP, mmHg	93 [83-103]	73 [70-82]	**<0.001**	93 [83-103]	73 [72-97]	**0.046**
Heart rate, beats/min	100 [100-110]	110 [92-125]	0.215	100 [100-110]	100 [96-118]	0.935
LVEDV, mL	210	210	0.275	210	214	**<0.001**

	[192-216]	[210-216]		[190-216]	[210-218]	
LVESV, mL	132 [121-148]	150 [140-150]	**0.003**	132 [120-140]	150 [140-160]	**<0.001**
LVEF, %	36.0 [31.0-38.0]	29.0 [29.0-35.0]	**0.004**	36.0 [32.0-38.0]	29.0 [27.0-35.0]	**<0.001**
TAPSE, mm	18 [13-19]	11 [10-14]	**<0.001**	18 [13-19]	15 [10-19]	0.053
HGI	0.62 [0.30-1.38]	4.16 [1.38-4.16]	**<0.001**	0.43 [0.26-0.85]	2.54 [1.40-4.16]	**<0.001**
GWTG-HF score, points	26 [20-44]	67 [38-67]	**<0.001**	22 [19-30]	60 [53-67]	**<0.001**

19 patients died during hospitalization and 39 patients experienced the prespecified composite adverse in-hospital outcome. Patients who died demonstrated a higher-risk clinical phenotype characterized by greater metabolic burden, poorer hemodynamic status, and impaired ventricular function ***(Table 2).*** Mortality was associated with higher BMI and glycemic indices, diabetes, smoking, ischemic heart disease, and dyslipidemia, alongside lower blood pressure, LVEF, TAPSE, and albumin. Both HGI and GWTG-HF scores were substantially higher among patients who died. Similar but broader differences were observed for the adverse composite ***(Table 2),*** encompassing metabolic, renal, hepatic, and cardiac abnormalities. HGI and GWTG-HF again showed particularly strong separation between patients with and without adverse events.

Table (3): Logistic regression for in-hospital all-cause mortality

Predictor	**Univariable OR (95% CI)**	**P-value**	**Adjusted OR (95% CI)**	**P-value**
Age, per 10 years	1.55 (0.96-2.52)	0.075	-	-
Male sex, male vs female	6.85 (1.52-30.96)	**0.012**	-	-
Active smoker	5.70 (1.79-18.22)	**0.003**	-	-
Hypertension	1.44 (0.54-3.84)	0.461	-	-
Diabetes mellitus	6.62 (1.83-23.90)	**0.004**	-	-
Chronic kidney disease	0.58 (0.18-1.87)	0.364	-	-
Ischemic heart disease	11.84 (1.53-91.61)	**0.018**	-	-
Dyslipidemia	8.64 (1.91-39.04)	**0.005**	-	-
BMI, per 5 kg/m^2	13.43 (4.28-42.16)	**<0.001**	-	-
Serum creatinine, per 1 mg/dL	0.64 (0.36-1.15)	0.137	-	-
Creatinine clearance, per 10 mL/min	1.07 (0.89-1.29)	0.487	-	-
Albumin, per 1 g/dL	0.15 (0.05-0.44)	**<0.001**	0.23 (0.07-0.74)	**0.014**
Potassium, per 1 mmol/L	0.62 (0.26-1.50)	0.289	-	-
Hemoglobin, per 1 g/dL	1.12 (0.81-1.54)	0.498	-	-
WBC count, per 1 ×10^9/L	1.25 (1.02-1.53)	**0.033**	-	-
Platelet count, per 50 ×10^9/L	1.18 (0.91-1.52)	0.215	-	-
SBP, per 10 mmHg	0.52 (0.37-0.74)	**<0.001**	-	-
DBP, per 10 mmHg	0.40 (0.24-0.69)	**<0.001**	-	-
MAP, per 10 mmHg	0.44 (0.28-0.69)	**<0.001**	-	-
Heart rate, per 10 beats/min	1.67 (1.04-2.67)	**0.033**	-	-
LVEDV, per 10 mL	1.58 (0.96-2.59)	0.073	-	-
LVESV, per 10 mL	1.47 (1.07-2.02)	**0.016**	-	-
LVEF, per 5 percentage points	0.54 (0.33-0.89)	**0.015**	-	-
TAPSE, per 1 mm	0.72 (0.62-0.85)	**<0.001**	-	-
Fasting blood glucose, per 10 mg/dL	1.79 (1.35-2.38)	**<0.001**	-	-
Baseline HbA1c, per 1%	1.90 (1.46-2.47)	**<0.001**	-	-
HGI, per 1 unit	2.34 (1.66-3.30)	**<0.001**	2.16 (1.51-3.10)	**<0.001**
GWTG-HF score, per 5 points	1.38 (1.19-1.60)	**<0.001**	-	-

In multivariable analysis, HGI remained independently associated with mortality after accounting for eligible nonredundant covariates (adjusted OR 2.16 per unit increase, 95% CI 1.51-3.10; P<0.001), while albumin remained independently protective ***(Table 3).***

Table (4): Logistic regression for in-hospital adverse clinical outcome

Predictor	Univariable OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age, per 10 years	1.22 (0.86-1.73)	0.263	-	-
Male sex, male vs female	2.43 (1.07-5.50)	**0.034**	-	-
Active smoker	2.19 (1.03-4.65)	**0.041**	-	-
Hypertension	1.43 (0.68-3.01)	0.347	-	-
Diabetes mellitus	16.50 (5.42-50.20)	**<0.001**	-	-
Chronic kidney disease	1.71 (0.78-3.74)	0.177	-	-
Ischemic heart disease	2.65 (1.11-6.34)	**0.029**	-	-
Dyslipidemia	5.69 (2.30-14.09)	**<0.001**	11.63 (2.75-49.19)	**<0.001**
BMI, per 5 kg/m^2	9.87 (4.30-22.64)	**<0.001**	-	-
Serum creatinine, per 1 mg/dL	1.34 (0.99-1.82)	0.058	-	-
Creatinine clearance, per 10 mL/min	0.88 (0.78-1.01)	0.067	-	-
Albumin, per 1 g/dL	0.99 (0.90-1.09)	0.825	-	-
Potassium, per 1 mmol/L	1.03 (0.52-2.01)	0.940	-	-
Hemoglobin, per 1 g/dL	0.79 (0.60-1.04)	0.095	-	-
WBC count, per 1 ×10^9/L	0.93 (0.81-1.08)	0.340	-	-
Platelet count, per 50 ×10^9/L	1.04 (0.87-1.25)	0.649	-	-
SBP, per 10 mmHg	0.77 (0.63-0.94)	**0.012**	-	-
DBP, per 10 mmHg	0.73 (0.53-0.99)	**0.044**	-	-
MAP, per 10 mmHg	0.73 (0.56-0.95)	**0.022**	-	-
Heart rate, per 10 beats/min	1.07 (0.74-1.55)	0.716	-	-
LVEDV, per 10 mL	2.06 (1.37-3.11)	**<0.001**	-	-
LVESV, per 10 mL	1.95 (1.47-2.59)	**<0.001**	-	-
LVEF, per 5 percentage points	0.35 (0.23-0.55)	**<0.001**	-	-
TAPSE, per 1 mm	0.89 (0.80-0.98)	**0.024**	1.47 (1.14-1.89)	**0.003**
Fasting blood glucose, per 10 mg/dL	2.04 (1.58-2.65)	**<0.001**	-	-
Baseline HbA1c, per 1%	2.25 (1.70-2.99)	**<0.001**	-	-
HGI, per 1 unit	2.90 (1.98-4.25)	**<0.001**	3.34 (1.96-5.72)	**<0.001**
GWTG-HF score, per 5 points	1.53 (1.34-1.76)	**<0.001**	-	-

The final mortality model demonstrated good discrimination (AUC 0.846). HGI likewise independently predicted the adverse composite (adjusted OR 3.34, 95% CI 1.96-5.72; P<0.001), alongside dyslipidemia and low TAPSE values ***(Table 4).***

Table (5): Association of HGI with GWTG-HF score and graded clinical risk across HGI quartiles

Measure	Q1 (≤0.34)	Q2 (>0.34-0.64)	Q3 (>0.64-1.46)	Q4 (>1.46)	P-value
Death	1 (2.9%)	2 (5.7%)	3 (8.6%)	13 (37.1%)	**<0.001**
Adverse composite	2 (5.7%)	2 (5.7%)	8 (22.9%)	27 (77.1%)	**<0.001**
Cardiac death	0 (0.0%)	0 (0.0%)	2 (5.7%)	9 (25.7%)	**<0.001**
Cardiogenic shock	0 (0.0%)	1 (2.9%)	2 (5.7%)	18 (51.4%)	**<0.001**
Myocardial infarction	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (11.4%)	**0.007**
VT/VF	0 (0.0%)	0 (0.0%)	1 (2.9%)	6 (17.1%)	**0.001**
Stroke	0 (0.0%)	1 (2.9%)	2 (5.7%)	1 (2.9%)	0.366
AKI	2 (5.7%)	0 (0.0%)	1 (2.9%)	10 (28.6%)	**0.001**
GWTG-HF score, median [IQR]	19 [19-20]	20 [20-24]	38 [30-44]	65 [60-67]	**<0.001**
<1%	35 (100.0%)	35 (100.0%)	14 (40.0%)	0 (0.0%)	**<0.001**
5-<10%	0 (0.0%)	0 (0.0%)	14 (40.0%)	0 (0.0%)	
10-<20%	0 (0.0%)	0 (0.0%)	7 (20.0%)	14 (40.0%)	
≥20%	0 (0.0%)	0 (0.0%)	0 (0.0%)	21 (60.0%)	

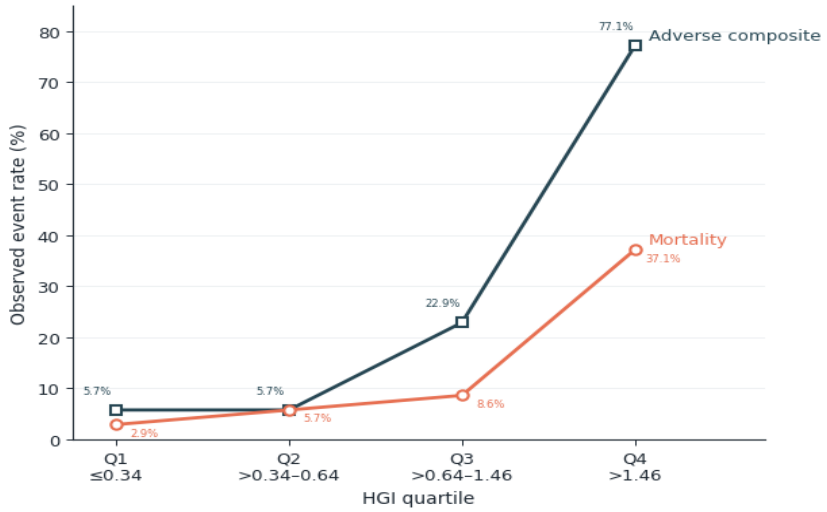

Figure 2. Clinical outcomes across HGI quartiles. Observed rates of in-hospital mortality and the adverse composite increased progressively across HGI quartiles (P for trend <0.001 for both), with the highest event burden in the fourth quartile.

This model achieved an AUC of 0.899, collectively supporting HGI as a robust marker of short-term adverse clinical risk across both study endpoints. HGI was strongly correlated with GWTG-HF score (Spearman ρ=0.918, 95% CI 0.862-0.953; P<0.001), demonstrating close concordance with established heart-failure risk**.** Increasing HGI quartiles were accompanied by graded increases in mortality and the adverse composite, as well as cardiac death, cardiogenic shock, myocardial infarction, ventricular arrhythmia, and acute kidney injury ***(Table 5; Figure 2).*** GWTG-HF risk also increased progressively across HGI quartiles, supporting a dose-response relationship between HGI and clinical severity ***(Table 5).***

Table (6): Discrimination of HGI for in-hospital outcomes and outcome distribution using the mortality-derived HGI cutoff

Outcome	AUC (95% CI)	P value	Optimal HGI cutoff	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
In-hospital all-cause mortality	0.821 (0.710-0.932)	**<0.001**	2.54	68.4% (43.4-87.4)	87.6% (80.4-92.9)	46.4% (27.5-66.1)	94.6% (88.7-98.0)
Adverse in-hospital composite	0.860 (0.779-0.941)	**<0.001**	1.28	87.2% (72.6-95.7)	78.2% (68.9-85.8)	60.7% (46.8-73.5)	94.0% (86.7-98.0)

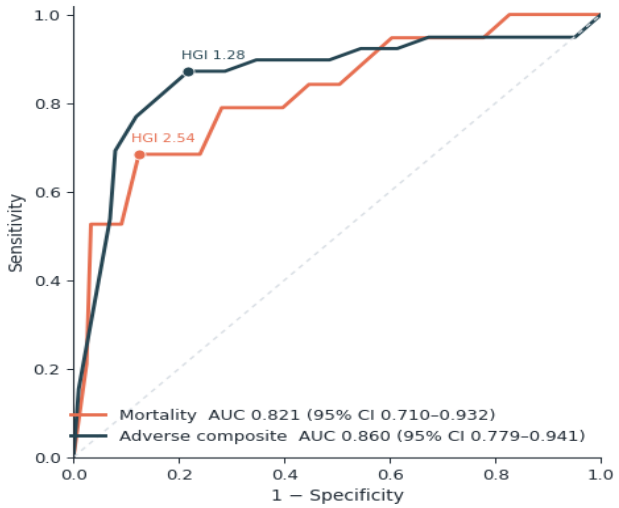

Figure 3. Discrimination of HGI for in-hospital outcomes. Receiver operating characteristic curves for mortality and the adverse composite. HGI yielded AUCs of 0.821 and 0.860, respectively. Youden-optimal HGI cutoffs were 2.54 for mortality and 1.28 for the adverse composite.

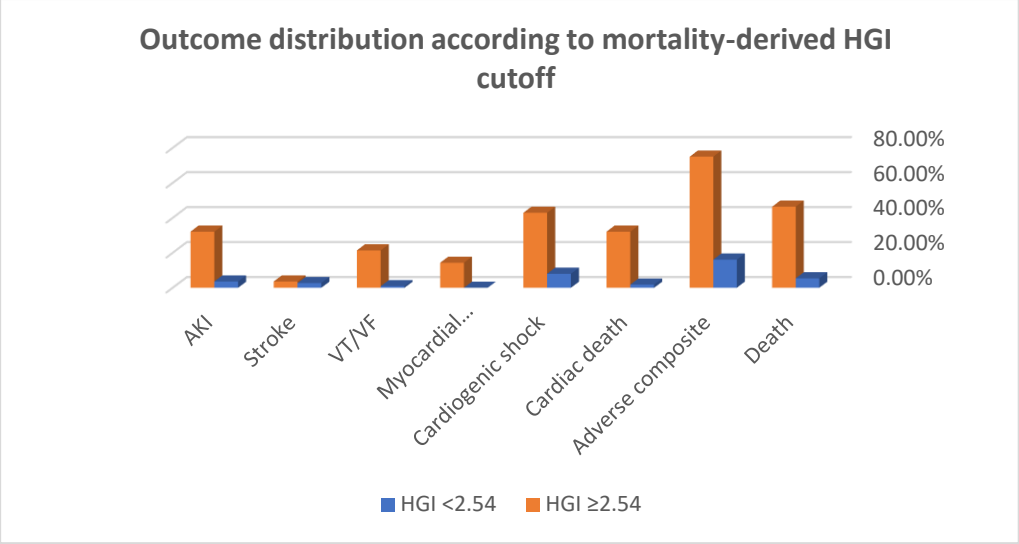

Figure 4. HGI ≥2.54 identified an increased odds ratio of mortality, the adverse composite, cardiac death, cardiogenic shock, ventricular arrhythmia and acute kidney injury. The stroke was not significantly associated with this value.

HGI demonstrated good discrimination for both mortality and the adverse composite ***(Table 6; Figure 3).*** Discrimination for mortality yielded an AUC of 0.821 (95% CI 0.710-0.932), with an optimal cutoff of 2.54. Performance was slightly stronger for the adverse composite (AUC 0.860, 95% CI 0.779-0.941), for which the optimal cutoff was 1.28. When the mortality-derived cutoff was applied clinically ***(Figure 4),*** HGI ≥2.54 identified a markedly higher-risk subgroup, with substantially increased odds of mortality, the adverse composite, cardiac death, cardiogenic shock, ventricular arrhythmia, and acute kidney injury; stroke was not significantly associated with this threshold.

DISCUSSION

Acute decompensated heart failure (ADHF) is one of the worldwide leading hospital admissions. Patients admitted with ADHF usually have a high in-hospital morbidity and mortality [10]. The measurement of HGI in all patients admitted to the hospital with ADHF is associated with an informative value for the prognosis and clinical outcome in these patients [11]. The present study showed that the most common co-morbidity distribution was ischemic heart disease (65%). In the same line with our findings, **Chioncel et al. [4]** who reported that ischemic cardiomyopathy is the most common leading cause of heart failure in between the hospitalized patients. Our results demonstrated that HGI and GWTG-HF scores were substantially higher among patients who died and increasing HGI quartiles were accompanied by graded increases in mortality and adverse clinical outcome, as well as cardiac death, cardiogenic shock, myocardial infarction, ventricular arrhythmia, and acute kidney injury**.** GWTG-HF risk also increased progressively across HGI quartiles, supporting a dose-response relationship between HGI and clinical deterioration. A high HGI is often accompanied by chronic inflammation and oxidative stress through advanced glycation end products (AGE) accumulation which affect the cardiovascular system and cause myocardial apoptosis, fibrosis, endothelial dysfunction and aggravating cardiac insufficiency. These findings were in concordance with **Ahn et al. [12]** who have suggested that chronic low-grade inflammation is more prevalent in patients with a high HGI thereby contributing to adverse outcomes and a higher incidence of in-hospital complications in patients admitted with ADHF. In multivariable analysis, HGI remained independently associated with mortality after accounting for eligible nonredundant covariates (adjusted OR 2.16 per unit increase, 95% CI 1.51-3.10; P<0.001), while albumin remained independently protective, as patients with ADHF often experience loss of protein. The reduction in serum albumin abolishes its competitive inhibition of HGB glycation, leading to an increase in HbA1c formation at the same levels of blood glucose and leading to a falsely increased HGI value [13]. In this analysis, reduced albumin levels are observed in non-survivors due to acceleration in the glycation process of hemoglobin. In this hospitalized ADHF cohort, the HGI values above cut-off value (2.54%) had a sensitivity of 68.4% and specificity of 87.6% (AUC=0.821, P value<**0.001**) to predict in-hospital mortality and the HGI values above cut-off value (1.28%) had a sensitivity of 87.2% and specificity of 78.2% (AUC=0.860, P value<**0.001**) to predict cardiogenic shock, acute kidney injury, life threatening arrhythmia, myocardial infarction, cerebrovascular stroke in between the patients admitted with acute decompensated heart failure during their hospital course. However, many studies discussed the value of HGI as a continuous risk marker for glycemia burden accumulation that drives acute decompensated heart failure disease to a lot of critical in-hospital adverse clinical outcomes, these studies failed to serve a clear threshold level of HGI for in-hospital mortality and adverse clinical outcome prediction in between hospitalized patients with ADHF [14]. The current research was the first study that succussed to give accurate levels of HGI for risk stratification, prediction in-hospital mortality and other adverse clinical outcomes in patients admitted with ADHF.

CONCLUSION

Our analysis demonstrated that an elevated HGI is independently associated with the risk of in-hospital mortality and other adverse clinical outcomes in the patients hospitalized with ADHF.

Limitations: This study was a single-center prospective cohort study, associated with many selection biases and the participants who were hospitalized with ADHF, did not have active myocardial ischemia or other acute diseases. Therefore, generalization of these results to other populations is limited.

Recommendations: In future studies, the HGI could be studied in a larger and more heterogeneous population to investigate its role in clinical decision-making and outcome improvement, and explore how the HGI interacts with heart failure guidelines-based therapy.

DECLARATIONS

Author Contributions: Methodology development: M.farouk. and Mohamed.G.Elbahnasawy.; clinical supervision: M.farouk., A.abdelaal., and Mohamed.G.Elbahnasawy.; data interpretation: A.abdelaal.; study conception: H.abdelatif. and Mohamed.G.Elbahnasawy.; patient recruitment, data collection, data organization, literature review, and manuscript drafting: H.abdelatif.; methodology review and clinical interpretation: Mohamed.G.Elbahnasawy.; critical manuscript revision: M.farouk., H.abdelatif, A.abdelaal. and Mohamed.G.Elbahnasawy .; all authors approved the final version of the manuscript and accept responsibility for the accuracy and integrity of the work.

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