ISSN 2618-1584 Vol. 7, Issue 4: 116-121, DOI: 10.25236/FMSR.2025.070415

Hemodynamic Gain Index and MACE Incidence-Prognostic and Preventive Value

Ying Hu, Yang Zhao*, Mengwen Yu, Jiayue Fei, Lina Wang

The Fifth Affiliated Hospital of Zhengzhou University, Zhengzhou, 450052, China
**Corresponding author: z13503846269@163.com*

Abstract: *The Hemodynamic Gain Index (HGI) is a parameter assessed during cardiopulmonary exercise testing (CPX). This study evaluated the association between HGI and the occurrence of Major Adverse Cardiovascular Events (MACE). This retrospective analysis included 211 patients who underwent CPX at the Fifth Affiliated Hospital of Zhengzhou University between January 2019 and January 2022. Patients were divided into quartile groups based on HGI percentile (calculated as [(HRpeak × SBPpeak) − (HRrest × SBPrest)] / (HRrest × SBPrest)). Baseline characteristics, laboratory findings, and long-term prognosis (MACE) were compared across groups. A predictive model incorporating three risk factors—"interventricular septal thickness, HGI, and history of diabetes"—was constructed. Receiver operating characteristic (ROC) curve analysis demonstrated that the performance of this model was superior to using peak oxygen consumption ($PeakVO_2$) alone for predicting MACE (AUC=0.787, 95% CI: 0.629-0.755 vs. AUC=0.637, 95% CI: 0.365-0.923; p=0.004). The predictive model developed in this study, comprising HGI, interventricular septal thickness, and history of diabetes, demonstrated higher diagnostic efficacy for adverse cardiovascular events compared to using $PeakVO_2$ alone. This model holds greater clinical utility for predicting major adverse cardiovascular events.*

Keywords: *Hemodynamic Gain Index; Cardiopulmonary Exercise Testing; Predictive Model*

1. Introduction

China's aging population is increasingly prominent, and the group at risk for cardiovascular diseases (CVD) is large, becoming the greatest threat to adult mortality. The medical resource burden caused by major adverse cardiovascular events (MACE) has continued to increase over the past decade. The prevention and treatment of CVD remain a long and challenging task[1]. Cardiopulmonary function and exercise capacity are key indicators for evaluating the prognosis of MACE. The hemodynamic gain index (HGI) serves as a comprehensive marker of hemodynamic reserve, capturing the net gain in the heart rate-blood pressure product (the product of heart rate [HR] and systolic blood pressure [SBP]) from rest to peak exercise[2]. HGI may become a critical indicator for assessing patients' exercise capacity and the risk of cardiovascular events. The aim of this study is to verify the correlation between HGI and exercise capacity parameters obtained from cardiopulmonary exercise testing (CPX), explore the predictive value of HGI in MACE events, and construct a cardiovascular event prediction model and nomogram, providing an objective, quantitative evaluation of the impact of various factors.

2. Materials and Methods

2.1 Study Subjects

From January 2019 to April 2022, 211 patients who underwent cardiopulmonary exercise testing (CPX) at the Fifth Affiliated Hospital of Zhengzhou University were included. The hemodynamic gain index (HGI) was calculated based on CPX parameters, and descriptive statistical grouping of HGI was performed using the 25th, 25th to 50th, 50th to 75th, and above the 75th percentiles. The predictive and prognostic value of the hemodynamic gain index in relation to cardiovascular event incidence was analyzed.

Inclusion criteria:

a) Inpatients who participated in cardiopulmonary exercise testing;

ISSN 2618-1584 Vol. 7, Issue 4: 116-121, DOI: 10.25236/FMSR.2025.070415

b) Aged between 40 and 80 years.

Exclusion criteria:

a) Patients with cognitive dysfunction, psychological cognitive disorders, or those who were unwilling or unable to cooperate during the experiment;

b) Malignant tumors (short life expectancy);

c) Patients with incomplete statistical or follow-up data;

d) Patients who refused to participate in the study.

2.2 Research Methods

2.2.1 Cardiopulmonary Exercise Testing

The Quark PFT Ergo cardiopulmonary exercise testing system, manufactured by COSMED S.R.L, Italy, was used.

2.2.2 Data Collection

Cardiopulmonary exercise testing indicators included: resting systolic blood pressure (SBPrest), resting diastolic blood pressure (DBPrest), resting heart rate (HRrest), peak oxygen uptake (PeakVO2/Kg), anaerobic threshold (AT), peak systolic blood pressure (SBPpeak), peak diastolic blood pressure (DBPpeak), peak heart rate (HRpeak), heart rate reserve (HRR), carbon dioxide ventilation equivalent (VE/VCO2), slope of carbon dioxide ventilation equivalent (VE/VCO2 slope), V, and HGI. Baseline indicators included: age, gender, blood lipids, BMI, medical history, smoking history, alcohol history, past medical history, use of hemodynamic improvement medications, and carotid plaque status.

2.2.3 Follow-up and Endpoint Events

Follow-up was conducted through the hospital's inpatient and outpatient systems or by telephone to confirm whether cardiovascular adverse events (MACE) occurred after patient discharge. MACE included unstable angina, recurrent myocardial infarction, heart failure, severe arrhythmia, and sudden cardiac death.

2.3 Statistical Methods

This study primarily used SPSS 27.0 and R (4.3.3) software for statistical analysis. Normally distributed continuous data were expressed as ±s. For homogeneity of variance, independent sample t-tests were used for group comparisons, and approximate t-tests were used for unequal variance. Skewed distribution data were expressed as M [P25;P75] and compared using the non-parametric Mann-Whitney U test. Categorical data were expressed as counts (n), with group comparisons performed using the chi-square test (Fisher's exact test was used for multiple rows and columns). The non-parametric Mann-Whitney U test was also used for comparisons of ranked data between two groups. Multivariate logistic regression analysis was used to construct a risk prediction model based on variables with $P<0.05$, and a nomogram was created for visual representation of the model. The performance of the prediction model was validated using the receiver operating characteristic (ROC) curve. All statistical analyses were two-sided, with $P<0.05$ considered statistically significant.

3. Results

3.1 Baseline Information

A total of 211 patients were included and divided into four groups based on HGI percentiles: "HGI1,HGI2, HGI3, HGI4," with 53, 56, 50, and 52 patients in each group, respectively. Statistical analysis was performed on the baseline data of the four groups. Significant differences were found in age ($p=0.000$), peak oxygen uptake ($p<0.001$), Peak O2 ($p<0.001$), HRR ($p<0.001$), Peak CO ($p<0.001$), and interventricular septal thickness ($p=0.007$). No statistically significant differences were found for the other results (Table 1).

Chi-square or Fisher's exact test was used to compare categorical variables (if applicable); the Kruskal-Wallis test was used to compare continuous variables; non-parametric data were analyzed using non-parametric tests; Q1 = 25th percentile; Q3 = 75th percentile;LDL: Low-Density Lipoprotein;

ISSN 2618-1584 Vol. 7, Issue 4: 116-121, DOI: 10.25236/FMSR.2025.070415

HDL: High-Density Lipoprotein.

Table 1 Baseline Data of HGI

	total (n=211)	HGI4 (>2.0) (n=53)	HGI3 (2.0-1.5) (n=56)	HGI2 (1.18-1.5) (n=50)	HGI1 (<1.18) (n=52)	P*
Age(n)	56.7±10.7	50.8±9.7	57.5±9.9	57.8±10.2	60.9±9.1	0.0001
female(n)	144	37	41	37	29	0.3958
BMI	25.38±3.3	25.57±3.5	24.92±2.4	24.90±3.2	26.10±3.9	0.2517
Drug(n)						0.8383
Yes	62	14	15	16	17	
No	149	39	41	34	35	
Smoking(n)						0.2118
Yes	70	16	14	17	23	
No	141	37	42	33	29	
Diabetes(n)						0.4013
Yes	24	4	5	6	9	
No	187	49	51	44	43	
Atrial fibrillation(n)						0.1360
Yes	8	0	1	3	4	
No	202	53	55	47	48	
Hypertension(n)						
Yes	86	16	20	26	24	0.3399
No	125	36	30	30	29	
Lipoprotein	85.70(33.60, 161.20)	76.60(40.20, 156.95)	82.25(24.52, 142.75)	73.80(26.30, 216.00)	107.25(40.25, 183.40)	0.7004
Apolipoprotein B	0.79(0.64, 9, 96)	0.78(0.56, 0.97)	0.81(0.645, 0.97)	0.78(0.62, 0.98)	0.78(0.64, 0.96)	0.8252
Triglycerides	1.60(1.09, 2.21)	1.60(0.92, 2.04)	1.72(1.10, 2.49)	1.45(1.09, 2.00)	1.70(1.09, 3.20)	0.2303
LDL	2.29(1.89, 2.89)	2.54(1.95, 2.95)	2.41(2.05, 2.90)	2.28(1.69, 2.93)	2.13(1.85, 2.55)	0.1247
HDL	1.19(1.00, 1.37)	1.23(1.04, 1.43)	1.21(1.00, 1.37)	1.19(1.06, 1.36)	1.12(0.95, 1.35)	0.3178
Total Cholesterol	4.54 ±1.08	4.76 ±1.15	4.60 ±1.09	4.42±1.11	4.35 ±0.95	0.5154
Interventricular Septum Thickness						
≥12mm	30	2	8	6	14	0.007
8-11mm	181	51	48	44	38	
Carotid Plaque Count						0.4207
≥3	25	9	4	5	7	
<3	186	44	52	45	45	
NYHA						0.1339
I	51	11	9	12	19	
II	127	30	38	33	26	
III	32	12	9	5	6	
IV	1	0	0	0	1	
peakO_2	17.30(15.30, 19.40)	19.00(17.35, 21.40)	18.2(16.10, 19.40)	16.60(15.38, 18.22)	14.65(12.95, 17.00)	<0.001
Peak O_2	1.24(1.04, 1.46)	1.05 (0.86, 1.31)	1.21 [1.11, 1.37]	1.24 [1.08, 1.50]	1.41 [1.21, 1.60]	<0.001
VE/VCO_2 slope	23.12(20.90, 25.80)	22.07(19.76, 24.39)	22.67(20.37, 25.94)	23.5(21.26, 26.13)	24.5(21.72, 28.00)	0.027
HRR	33.4±16.32	24.85±13.86	28.22 ±14.75	35.66±14.55	46.28±13.49	<0.001
Peak O_2 pulse	9.72±2.27	9.93±2.06	9.74±2.12	9.62±2.25	9.56±2.66	<0.001
Peak CO	8.24(6.92, 9.63)	9.39(8.14, 10.93)	8.13(7.15, 9.79)	8.11(7.32, 9.04)	7.03(5.74, 8.70)	<0.001
AT	12.30(10.70, 13.60)	11.60(9.82, 13.00)	11.50 (10.57, 12.67)	12.70(11.25, 14.55)	12.90(11.80, 13.70)	<0.001

3.2 Univariate Analysis and Multivariate Logistic Regression

Univariate analysis identified significant variables, and further multivariate binary logistic regression (stepwise method) was used to select independent influencing factors. The “rms” package in R software was used to create a nomogram prediction model, and ROC curves were drawn (Figures 1 and 2).

3.2.1 Construction of the Nomogram Prediction Model

The nomogram prediction model was constructed based on the three independent influencing factors identified by logistic regression analysis. The nomogram is based on each regression coefficient, which is proportionally converted into a scale from 0 to 100 points. These points are summed according to the independent variables, and the total score is used to locate the position on the total score scale. The higher the total score, the greater the risk. The influencing factors included HGI, interventricular septal thickness, and history of diabetes.

3.2.2 ROC Curve

ROC curves were plotted to analyze the model’s diagnostic efficiency for cardiovascular event occurrence. The results showed that the model (Figure 2A) had an AUC of 0.787 (95% CI: 0.629–0.755). When using peak oxygen uptake alone to diagnose cardiovascular event occurrence, the

ISSN 2618-1584 Vol. 7, Issue 4: 116-121, DOI: 10.25236/FMSR.2025.070415

model's AUC for Peak VO2 (Figure 2B) was 0.637 (95% CI: 0.558–0.715). The diagnostic efficiency of the prediction model was better than using Peak O2 alone (p=0.004). The Hosmer-Lemeshow test showed good goodness-of-fit ($\chi 2$=10.36, P=0.24). The clinical decision curve demonstrated that the prediction model has good clinical application value.

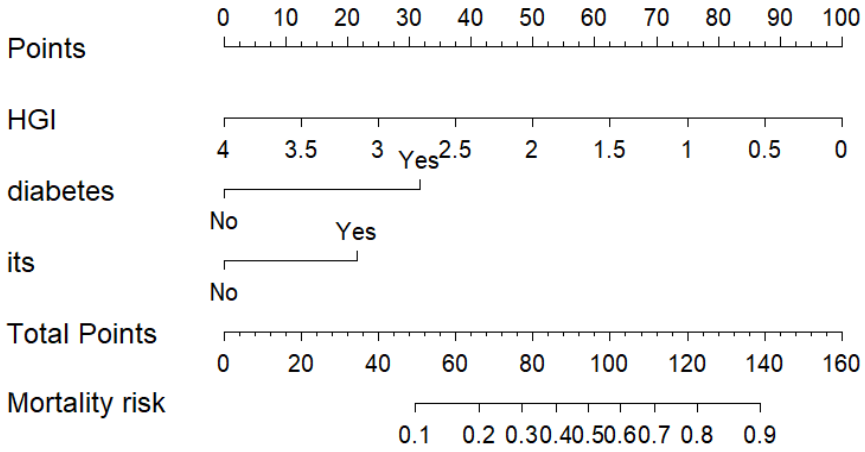
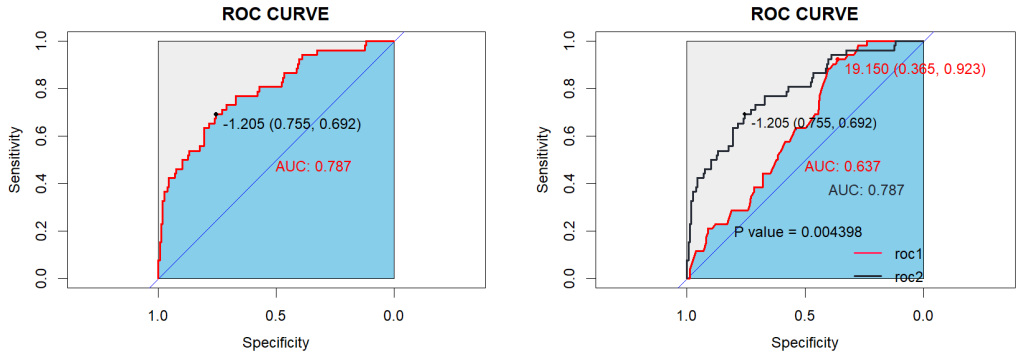
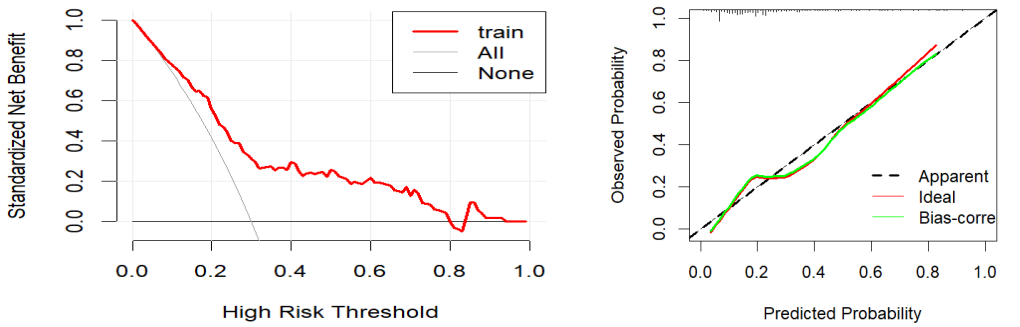


Figure 1 Nomogram Prediction Model

Note: age = age, yes (greater than 60), no (less than or equal to 60); its = interventricular septal thickness, yes (greater than 12), no (less than or equal to 11); arrhythmia = arrhythmia, yes (history of arrhythmia), no (no history of arrhythmia); diabetes = diabetes, yes (history of diabetes), no (no history of diabetes)



A: ROC Curve of the Prediction Model B: ROC Curve of the Prediction Model and Peak Oxygen Uptake



C: Clinical Decision Curve Analysis of the Nomogram Prediction Model D: Calibration Curve of the Nomogram Prediction Model

Figure 2: roc1 represents the Peak O2 curve, and roc2 represents the prediction model curve.

4. Discussion

Cardiopulmonary exercise testing (CPX) is a well-established clinical examination that provides

ISSN 2618-1584 Vol. 7, Issue 4: 116-121, DOI: 10.25236/FMSR.2025.070415

valuable diagnostic and prognostic information for patients with various chronic diseases[3]. Cardiovascular disease (CVD) remains the leading cause of death worldwide[4]. Although CVD mortality has declined in recent years, hospital admissions due to acute manifestations of major adverse cardiovascular events (MACE) continue to rise. Physical inactivity is a major behavioral risk factor for CVD, and cardiopulmonary function is an important prognostic indicator[5]. As a simple parameter, the hemodynamic gain index (HGI) can be applied to predict the incidence of MACE and explore its prognostic and preventive value.

Hemodynamic responses during exercise testing are crucial for assessing cardiovascular function, diagnosing cardiovascular diseases, and evaluating overall prognosis[6]. HGI, as a comprehensive measure of hemodynamic reserve, captures the net gain in the heart rate–blood pressure product (the product of heart rate [HR] and systolic blood pressure [SBP]) from rest to peak exercise. Research by Baruch Vainshelboim et al. found that HGI is a strong predictor of heart failure (HF) incidence in men, supporting its prognostic value and indicating that higher HGI is independently associated with lower HF risk[2]. Another study confirmed that HGI in female patients also holds predictive and prognostic value for cardiovascular diseases[6].

Some observational studies have shown that CPX parameters, either directly measured or estimated through exercise testing, are negatively and independently associated with cardiovascular outcomes and type 2 diabetes[7,8]. Nesti L et al. reported that diabetic patients exhibit reduced peak oxygen uptake before the onset of significant cardiovascular events[9]. Cardiac remodeling is common among patients with HF and serves as an indicator of disease progression and severity. Interventricular septal hypertrophy is one aspect of remodeling. The septum plays a role in maintaining ventricular integrity and coordinating effective cardiac pumping. Abel N et al. found that septal hypertrophy was not associated with all-cause mortality over a median follow-up of 30 months but was independently predictive of rehospitalization risk. Moreover, septal hypertrophy was identified as a predictor of mortality, even among patients with a normal left ventricular mass index[10].

Based on data analysis, a prediction model was constructed using three risk factors—interventricular septum, HGI, and history of diabetes. The area under the ROC curve for this prediction model (AUC = 0.787, 95% CI: 0.629–0.755) was significantly higher than that of peak oxygen uptake (AUC = 0.637, 95% CI: 0.365–0.923) ($p = 0.004$). This model provides valuable reference for clinicians in predicting recurrent cardiovascular events and evaluating prognosis among high-risk populations.

β-blockers can impair heart rate response during exercise and may reduce HGI[2], yet no significant differences in HGI were observed across groups in this study, nor did β-blockers appear to significantly affect prognosis. Factors such as patient medication adherence and information bias cannot be ruled out. Additionally, this study lacked a broader range of cardiac structural indicators, suggesting the need for further investigation into the relationship between HGI and cardiac remodeling.

In conclusion, HGI is a parameter derived from routine exercise testing and can serve as a substitute for peak oxygen uptake, particularly suitable for treadmill tests where gas exchange analysis is not feasible. Incorporating HGI into prognostic assessments for high-risk patients and implementing cardiopulmonary fitness interventions in individuals with low HGI may strengthen current public health prevention strategies and offer a more precise and effective approach to patient health management.

References

[1] FAN J, SUN Z, YU C, et al. Multimorbidity patterns and association with mortality in 0.5 million Chinese adults[J]. Chin Med J (Engl), 2022,135(6): 648-657.

[2] VAINSHELBOIM B, KOKKINOS P, MYERS J. Prognostic Value and Clinical Usefulness of the Hemodynamic Gain Index in Men[J]. Am J Cardiol, 2019,124(4): 644-649.

[3] AHMADI M N, HAMER M, GILL J M R, et al. Brief bouts of device-measured intermittent lifestyle physical activity and its association with major adverse cardiovascular events and mortality in people who do not exercise: a prospective cohort study[J]. Lancet Public Health, 2023,8(10): e800-e810.

[4] VISSEREN F L J, MACH F, SMULDERS Y M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice[J]. Eur Heart J, 2021,42(34): 3227-3337.

[5] MOTIWALA S R, NAYOR M. Risk Stratification in Advanced Heart Failure: Can Simple Hemodynamic Indices Replace Comprehensive CPET?[J]. JACC Heart Fail, 2024,12(2): 272-274.

[6] VAINSHELBOIM B, MYERS J. Haemodynamic gain index and heart failure incidence- Prognostic

ISSN 2618-1584 Vol. 7, Issue 4: 116-121, DOI: 10.25236/FMSR.2025.070415

and preventive value[J]. Eur J Prev Cardiol, 2023,30(13): 1404-1411.
[7] LAUKKANEN J A, ISIOZOR N M, KUNUTSOR S K. Objectively Assessed Cardiorespiratory Fitness and All-Cause Mortality Risk: An Updated Meta-analysis of 37 Cohort Studies Involving 2,258,029 Participants[J]. Mayo Clin Proc, 2022,97(6): 1054-1073.
[8] KUNUTSOR S K, KHAN H, SEIDU S, et al. Percentage of Age-Predicted Cardiorespiratory Fitness May Be a Stronger Risk Indicator for Incident Type 2 Diabetes Than Absolute Levels of Cardiorespiratory Fitness[J]. J Cardiopulm Rehabil Prev, 2023,43(1): 66-73.
[9] ABEL N, SCHUPP T, ABUMAYYALEH M, et al. Prognostic Implications of Septal Hypertrophy in Patients with Heart Failure with Mildly Reduced Ejection Fraction[J]. J Clin Med, 2024,13(2).
[10] LONCARIC F, NUNNO L, MIMBRERO M, et al. Basal Ventricular Septal Hypertrophy in Systemic Hypertension[J]. Am J Cardiol, 2020,125(9): 1339-1346.