Original Article

Prognostic Value of the Naples Score for Identifying Patients with Implantable Cardioverter-Defibrillators at Risk of Malignant Ventricular Arrhythmias

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Abstract

Background: Ventricular arrhythmias, including ventricular tachycardia and ventricular fibrillation, are major causes of sudden cardiac death (SCD) in patients with structural heart disease. Implantable cardioverter-defibrillators (ICDs) are effective in preventing SCD; however, identifying patients at higher risk of malignant ventricular arrhythmias and appropriate ICD therapies remains challenging. The Naples score, a composite marker of systemic inflammation and nutritional status, has emerged as a prognostic indicator in various cardiovascular conditions.

Objectives: This study aimed to evaluate the predictive value of the Naples score for malignant ventricular arrhythmias and ICD shock therapy in patients undergoing ICD implantation for secondary prevention.

Methods: This retrospective study included 360 patients who underwent ICD implantation for secondary prevention due to ventricular arrhythmias associated with ischemic heart disease. Patients were categorized into two groups based on the occurrence of appropriate ICD therapy.

Results: During follow-up, malignant ventricular arrhythmias requiring ICD therapy occurred in 139 patients. The Naples score was significantly higher in patients who experienced ICD shocks compared to those who did not ($p = 0.027$). However, in multivariable analysis, the Naples score was not identified as an independent predictor of ICD shock.

Conclusions: Higher Naples scores were associated with malignant ventricular arrhythmias and ICD shocks at the univariable level. However, the Naples score had limited predictive accuracy and was not found to be an independent predictor in multivariable analysis. The clinical use of the Naples score should be interpreted with caution, and it should not be used as a standalone decision-making tool.

Keywords: Implantable Defibrillators; Cardiac Arrhythmias; Inflammation; Nutritional Status.

Introduction

Cardiovascular diseases remain one of the leading causes of mortality worldwide and impose a significant economic burden on healthcare systems due to their high morbidity.[1] These conditions can lead to numerous severe complications, including ventricular arrhythmias, atrial fibrillation, heart failure, valvular diseases, and left ventricular dysfunction. Among these, the most devastating and life-threatening complication is undoubtedly ventricular arrhythmia. Despite pharmacological treatments, the risk of sudden cardiac death (SCD) due to malignant arrhythmias remains high in certain patient populations.[2] To reduce this risk, implantable cardioverter-defibrillators (ICDs) have become a crucial device-based therapy for both primary and secondary prevention of SCD. ICDs are recommended for primary prevention in patients with reduced left ventricular ejection fraction (LVEF) and advanced heart failure[3] and for secondary prevention in those who have previously experienced episodes of ventricular tachycardia or ventricular fibrillation.[4] Although the mortality-reducing benefits of ICD therapy are well established, accurately identifying patients who will truly benefit from ICD implantation remains a major clinical challenge.[5] A substantial proportion of patients who receive ICDs do not receive any therapy from the device during follow-up. Nonetheless, ICD implantation may expose these patients to unnecessary procedural risks, device-related infections, psychological burden, or serious complications such as inappropriate shocks.[6,7] Therefore, improving risk stratification to better select appropriate candidates for ICD therapy is a critical need in current clinical practice.

In recent years, novel prognostic biomarkers and scoring systems have been investigated to enhance patient selection in various diseases. One such tool is the Naples score, an

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Central Illustration: Prognostic Value of the Naples Score for Identifying Patients with Implantable Cardioverter-Defibrillators at Risk of Malignant Ventricular Arrhythmias

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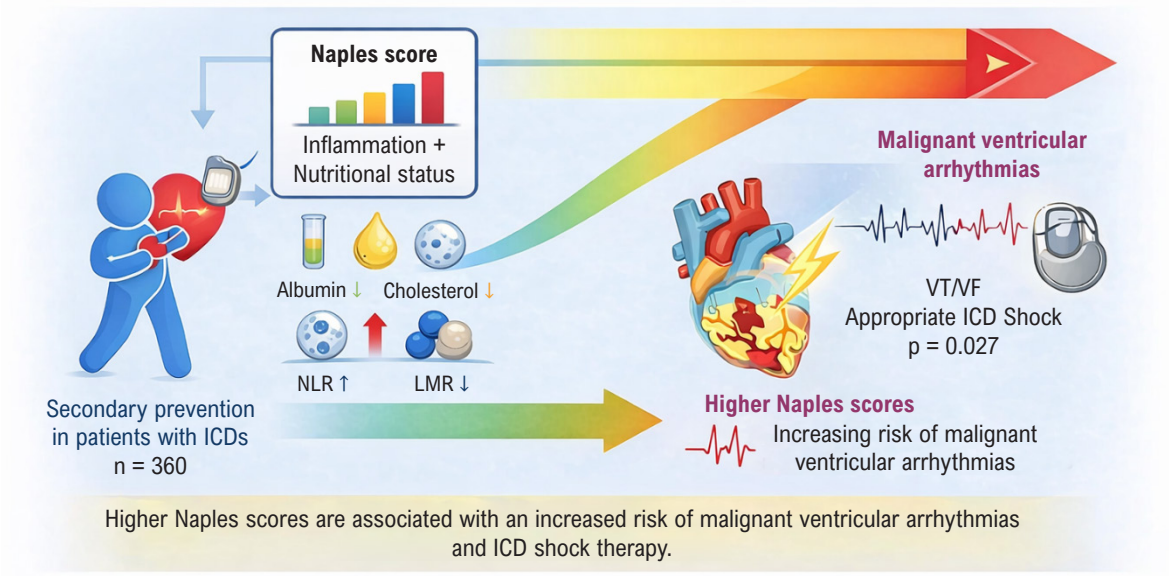

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Prognostic Value of the Naples Score for Identifying Patients with ICD at Risk of Malignant Ventricular Arrhythmias. ICD: implantable cardioverter-defibrillator; LMR: lymphocyte-to-monocyte ratio; NLR: neutrophil-to-lymphocyte ratio; VF: ventricular fibrillation; VT: ventricular tachycardia.

immunonutritional index that reflects systemic inflammation and nutritional status, incorporating parameters such as serum albumin, total cholesterol, neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR). Initially introduced in oncology and surgical patient populations, this score has also been suggested as a predictor of adverse outcomes in cardiovascular diseases.[8-10]

However, the role of the Naples score in predicting arrhythmic events or ICD shocks has not yet been studied. In this study, we aimed to investigate the potential association between the Naples score and ICD shocks in patients undergoing device implantation and to contribute to the improvement of current risk stratification strategies.

Methods

Patient population

Between January 2022 and January 2024, a total of 360 patients aged ≥ 18 years who underwent ICD implantation for secondary prevention due to ventricular arrhythmias in the setting of ischemic heart disease at our center were included in the study. All patients had at least two device follow-up visits at six-month intervals and a minimum post-implantation follow-up duration of one year. During follow-up, all therapies delivered in response to malignant ventricular arrhythmias, including antitachycardia pacing and shocks, were considered as ICD therapies. Inappropriate ICD therapies were excluded from the analysis. Demographic, clinical, and laboratory data were recorded at the time of device implantation for all patients.

The Naples score was calculated using serum albumin, total cholesterol, NLR, and LMR. Each parameter was assigned 0 or 1 point based on the following thresholds: serum albumin ≥ 4.0 g/dL = 0 points, < 4.0 g/dL = 1 point; total cholesterol ≥ 180 mg/dL = 0 points, < 180 mg/dL = 1 point; NLR ≤ 2.96 = 0 points, > 2.96 = 1 point; LMR > 4.44 = 0 points, ≤ 4.44 = 1 point. The total score ranged from 0 to 4.

In addition, basic electrocardiographic parameters (heart rhythm, QT interval, and heart rate) and echocardiographic parameters were obtained from patients' medical records. Based on whether ICD therapy was delivered or not, patients were divided into two groups: those who received ICD therapy (antitachycardia pacing and/or shock) and those who did not receive any ICD intervention during follow-up. The study was conducted in accordance with the principles of the 2013 Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol was reviewed and approved by the local ethics committee (decision number: 2025/5804, dated May 23, 2025).

Statistical analysis

Data entry and statistical analyses were performed using SPSS for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA).

The normality of data distribution was assessed using visual methods (histograms and probability plots) and analytical methods (Kolmogorov–Smirnov test). For numerical data, mean, standard deviation, and median (first–third quartiles) values were used; categorical data were summarized using frequency distributions and percentages.

Comparisons between numerical and categorical data were performed using the independent-samples t test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. The chi-squared test was used for comparisons of categorical variables. The diagnostic performance of the Naples score in predicting ICD shocks was evaluated using receiver operating characteristic (ROC) curve analysis. The optimal cutoff value was determined using the Youden index: max(sensitivity + specificity − 1). Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for the identified threshold.

Multivariable logistic regression was performed to evaluate the association between independent variables and ICD shocks. The model included age, sex, LVEF, presence of atrial fibrillation, glomerular filtration rate (GFR), left ventricular end-systolic diameter (LVESD), diabetes mellitus, and the Naples score.

All variables were entered simultaneously (enter method). Model significance was assessed using the omnibus test, and model calibration was evaluated with the Hosmer–Lemeshow goodness-of-fit test. The explanatory power of the model was expressed using the Nagelkerke R^2 coefficient. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Correlations between non-normally distributed variables were assessed using Spearman's correlation coefficient. A p value < 0.05 was considered statistically significant.

Results

A total of 360 patients were included in the study, comprising 221 patients who did not receive ICD shocks and 139 patients who did. There were no statistically significant differences between the shock and no-shock groups in terms of age and sex distribution ($p = 0.511$ and $p = 0.434$, respectively). Similarly, the frequency of comorbidities did not differ significantly between the two groups (all $p > 0.05$).

LVEF was significantly higher in patients without shocks ($p = 0.006$), whereas left atrial diameter and LVESD were significantly greater in patients who received shocks ($p = 0.008$ and $p = 0.027$, respectively). In addition, serum creatinine levels were significantly higher, and GFR, low-density lipoprotein (LDL), and total cholesterol levels were significantly lower in the shock group (all $p < 0.001$). No significant differences were observed between the groups in terms of other electrocardiographic, echocardiographic, or laboratory parameters ($p > 0.05$).

Implantation duration , number of device checks, and number of recurrent ICD therapies were significantly higher in patients who received shocks (all $p < 0.001$). The median Naples score was 2 in the no-shock group and 3 in the shock group, and this difference was statistically significant ($p = 0.027$) (Figure 1). Moreover, the rate of atrial fibrillation detection during device checks was significantly higher in the shock group (30.2%) compared to the no-shock group (13.6%) ($p < 0.001$). The distribution of troponin elevation was similar between the groups ($p > 0.05$). These findings are summarized in Table 1 and the Central Illustration.

The diagnostic ability of the Naples score to predict ICD shocks was evaluated using a ROC curve (Figure 2). The area under the ROC curve (AUC) values and corresponding cutoff points derived from the ROC analysis are presented in Table 2. According to the ROC analysis, the AUC value for the Naples score was calculated as 0.567 (95% CI: 0.506–0.628). This AUC value was found to be statistically significant ($p = 0.032$). According to the Youden index, the optimal cutoff value of ≥ 2 for the Naples score yielded a sensitivity of 81.3% and a specificity of 26.7%. For a cutoff value of ≥ 3, the sensitivity was 53.2%, and the specificity was 53.4%.

A multivariable logistic regression analysis was performed to identify predictors of ICD shock occurrence. In this analysis, the presence of atrial fibrillation detected during device follow-up was independently associated with ICD shock (OR: 2.615; 95% CI: 1.442–4.742; $p = 0.002$). Diabetes mellitus was found to be inversely associated with ICD shock (OR: 0.565; 95% CI: 0.329–0.972; $p = 0.039$). In contrast, age, sex, LVEF, LVESD, heart failure, GFR, and Naples score were not significantly associated with ICD shock (all $p > 0.05$), as shown in Table 3.

Discussion

Ventricular tachycardia and ventricular fibrillation occur more frequently in individuals with structural heart disease and are among the most lethal cardiac arrhythmias. Clinically, they may present with nonspecific symptoms such as syncope, dizziness, palpitations, dyspnea, or sudden loss of consciousness. These arrhythmias impair myocardial contractility, leading to an abrupt reduction in cardiac output and necessitating prompt and effective treatment. Ventricular fibrillation is one of the shockable rhythms of cardiac arrest and results in the complete loss of effective cardiac output, rapidly causing hemodynamic collapse. Ventricular tachycardia, on the other hand, is associated with hemodynamic instability, syncope, cardiogenic shock, and SCD. Therefore, early detection and prevention of ventricular arrhythmias—particularly in patients with structural heart disease—are crucial for reducing morbidity and improving survival.

Structural remodeling of the heart, particularly within the cardiac chambers, due to various underlying conditions provides a critical substrate for the development of arrhythmias. Whereas left atrial dilation is associated with an increased risk of atrial arrhythmias, left ventricular dilation is linked to ventricular arrhythmias.[11,12] The difference between LVESD and LVEDD can offer insights into the arrhythmogenic substrate. In our study, LVEF, left atrial diameter, and LVESD showed significant differences between groups. These findings support the notion that structural remodeling may be associated with an increased need for ICD therapy. Notably, while LVESD was statistically significant, LVEDD was not. This suggests that contractile dysfunction and systolic remodeling

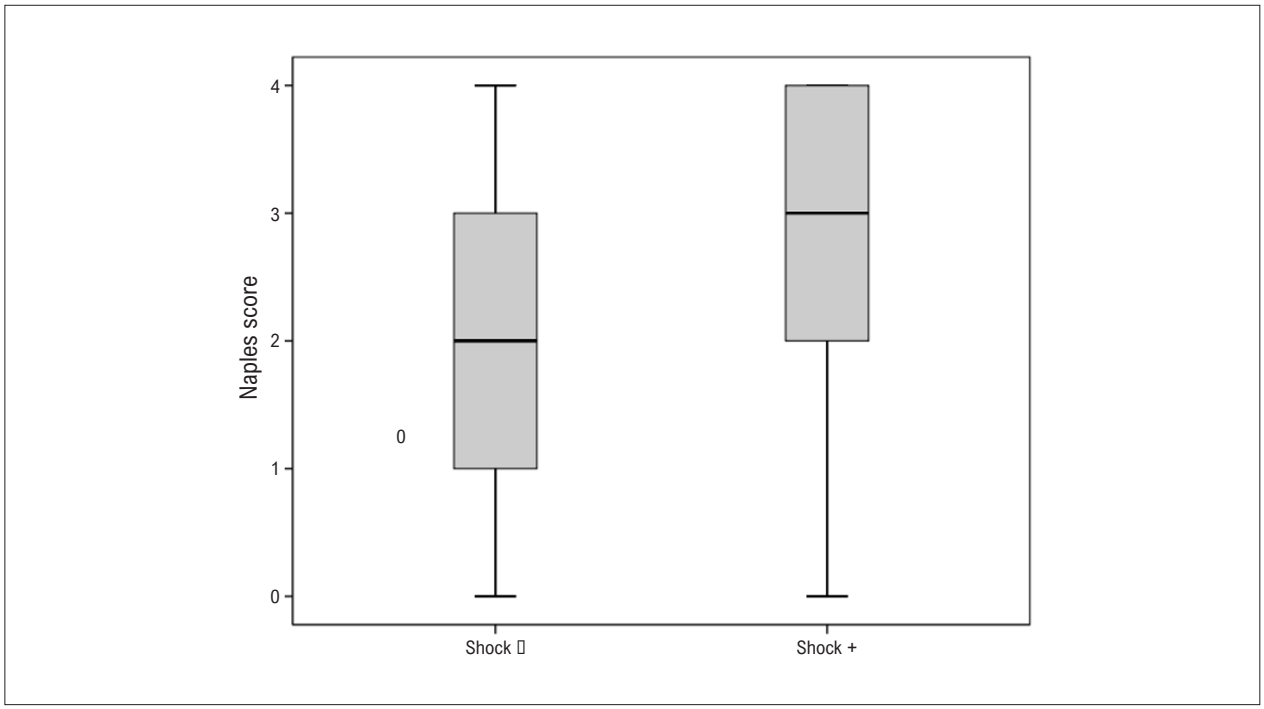

Figure 1 – *Distribution of Naples scores in patients with and without ICD shocks*

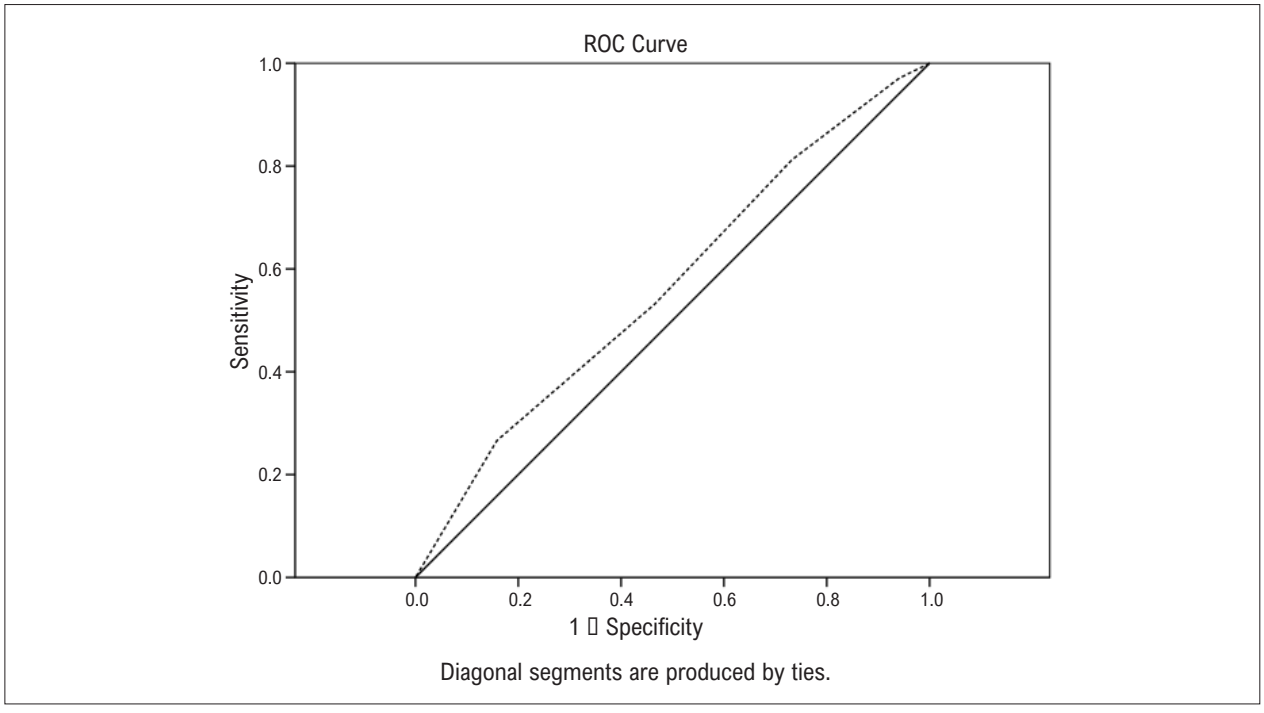

Figure 2 – *ROC curve for the predictive value of the Naples score in identifying ICD shocks. ROC: receiver operating characteristic. Higher scores indicate diagnostic relevance for patients who received shocks.*

may be more closely related to arrhythmogenic risk than mere chamber enlargement. Indeed, previous studies have also shown that systolic dilation is a stronger predictor of arrhythmic risk than diastolic dilation.[13]

Although cardiac structures and electrical abnormalities play a major role in the development of ventricular arrhythmias, various clinical characteristics, as well as metabolic and proinflammatory markers, also contribute to this

Table 1 – Comparison of demographic characteristics, comorbidities, echocardiographic, electrocardiographic, and laboratory parameters between patients with and without ICD shocks

Characteristic	No-shock group (n=221)	Shock group (n=139)	p
Age, mean ± SD	**63.54±12.98**	**64.47±13.19**	**0.511[a]**
Sex, n (%)			
Female	54 (24.4)	29 (20.9)	0.434[b]
Male	167 (75.6)	110 (79.1)	
Comorbidities, n (%)			
Heart failure	209 (94.6)	136 (97.8)	0.130[a]
Hypertension	113 (51.1)	73 (52.5)	0.798[a]
Diabetes mellitus	76 (34.4)	38 (27.3)	0.161[a]
History of stroke	16 (7.2)	12 (8.6)	0.631[a]
Vascular disease	4 (1.8)	3 (2.2)	0.551[a]
Renal failure	9 (4.1)	8 (5.8)	0.470[a]
	Mean ± SD	**Mean ± SD**	
QRS duration (ms)	109.71±35.64	112.07±38.76	0.564[a]
Heart rate (bpm)	71.05±14.09	69.62±15.10	0.376[a]
QT interval (ms)	413.80±50.15	410.87±44.10	0.581[a]
LVEF (%)	37.38±10.90	34.12±10.50	0.006[a]
Left atrial diameter (mm)	41.66±6.79	43.73±7.34	0.008[a]
LVEDD (mm)	56.02±8.69	57.95±10.33	0.064[a]
LVESD (mm)	40.82±10.66	43.63±11.64	0.027 [a]
PASP (mmHg)	36.33±11.75	37.55±11.13	0.351[a]
Hemoglobin (g/dL)	13.57±2.05	13.60±1.98	0.904[a]
WBC (×10³/μL)	8.75±3.15	9.03±3.40	0.427[a]
Platelet count (×10³/μL)	225.60±70.72	233.53±71.70	0.368[a]
Monocyte (×10³/μL)	0.67±0.24	0.74±0.38	0.064[a]
Neutrophil (×10³/μL)	5.87±3.03	6.23±3.34	0.297[a]
Lymphocyte (×10³/μL)	2.01±0.90	1.85±0.82	0.095[a]
Creatinine (mg/dL)	1.11±0.52	1.24±0.79	0.048[a]
GFR (mL/min/1.73 m²)	78.31±29.57	72.08±27.15	0.047[a]
Sodium (mmol/L)	138.23±4.38	138.17±3.94	0.907[a]
Potassium (mmol/L)	4.57±0.56	4.60±0.58	0.971[a]
Albumin (g/dL)	3.83±0.59	3.80±0.53	0.661[a]
Calcium (mg/dL)	9.03±0.70	9.03±0.56	0.974[a]
Magnesium (mg/dL)	2.02±0.30	2.08±0.28	0.089[a]
LDL (mg/dL)	101.77±36.89	92.54±35.51	0.020[a]
HDL (mg/dL)	40.55±12.63	38.68±10.09	0.142[a]
Triglycerides (mg/dL)	153.56±82.13	142.99±81.20	0.233[a]
Total cholesterol (mg/dL)	173.04±46.35	159.83±47.07	0.009[a]
Troponin (ng/mL)	2.72±16.48	0.65±2.25	0.119[a]

	Median (IQR)	Median (IQR)	
Implantation duration (months)	5 (3–7)	7 (5–9)	<0.001[c]
Number of device checks	5 (2–7)	7 (4–10)	<0.001[c]
Recurrent ICD therapy	0	3 (1–7)	<0.001[c]
Naples score	2 (1–3)	3 (2–4)	0.027[c]
	n (%)	**n (%)**	
Troponin elevation			
Absent	85 (55.6)	62 (54.9)	0.911[b]
Present	68 (44.4)	51 (45.1)	
AF during device check			
Absent	190 (86.4)	97 (69.8)	<0.001[b]
Present	30 (13.6)	42 (30.2)	

AF: atrial fibrillation; GFR: glomerular filtration rate; HDL: high-density lipoprotein; ICD: implantable cardioverter-defibrillator; IQR: interquartile range; LDL: low-density lipoprotein; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; PASP: pulmonary artery systolic pressure; SD: standard deviation; WBC: white blood cell count. [a] Independent-samples t test; [b] chi-squared test; [c] Mann–Whitney U test.

Table 2 – ROC analysis results for the Naples score

	AUC (95% CI)	p	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Naples score	0.567 (0.506–0.628)	0.032	≥2	81.3	26.7	41.1	69.4
			≥3	53.2	53.4	41.8	64.8

AUC: area under the receiver operating characteristic curve; CI: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

Table 3 – Multivariable logistic regression analysis identifying predictors of ICD shock

Variable	B	Standard error	OR, Exp(B)	95% CI	p
Age	−0.007	0.010	0.993	0.973–1.013	0.477
Sex (male)	0.228	0.307	1.256	0.688–2.293	0.457
LVEF	−0.028	0.018	0.973	0.940–1.007	0.113
LVESD	−0.002	0.016	0.998	0.967–1.030	0.879
Heart failure	0.583	0.854	1.791	0.336–9.558	0.495
Diabetes mellitus	−0.570	0.277	0.565	0.329–0.972	0.039
GFR	−0.007	0.005	0.993	0.984–1.002	0.148
Naples score	0.152	0.113	1.164	0.933–1.453	0.179
AF during device follow-up	0.961	0.304	2.615	1.442–4.742	0.002

AF: atrial fibrillation; CI: confidence interval; GFR: glomerular filtration rate; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; OR: odds ratio. All variables were entered into the multivariable model simultaneously using the enter method. Overall model significance was confirmed by the omnibus test ($\chi^2 = 29.493$; $p = 0.001$). Model calibration assessed by the Hosmer–Lemeshow test indicated good fit ($p = 0.146$). The explanatory power of the model was modest, with a Nagelkerke R^2 of 0.120.

process. Impaired renal function may increase susceptibility to cardiac arrhythmias. This is due to the fact that uremic toxins can disrupt myocardial electrical stability and electrolyte imbalances can create a substrate for arrhythmogenesis.[14] In the presence of structural heart disease, this process is further accelerated, making arrhythmia development more likely. Moreover, reduced GFR is also a marker of poor prognosis and increased inflammation.[15] These findings support the arrhythmogenic potential of renal dysfunction. However, in our study, although there was no clinically significant renal failure or electrolyte imbalance between groups, the significant difference in creatinine and GFR levels in the shock group may indicate the presence of subclinical renal dysfunction in individuals without overt renal failure. Even at this subclinical level, renal impairment may contribute to an increased susceptibility to ventricular arrhythmias.

Although ICDs have significantly improved outcomes in patients at risk of SCD, appropriate patient selection has become increasingly important. Inappropriate ICD implantation not only increases healthcare costs but also exposes patients to serious complications such as inappropriate shocks, lead dysfunction, infections, and psychological stress.[6,16] In this context, the development of simple, reliable, and cost-effective tools to improve risk stratification in ICD candidates represents an important clinical need.

In recent years, several risk stratification models have been developed to improve the identification of appropriate candidates for ICD therapy. The Seattle Proportional Risk Model (SPRM) aims to estimate the expected benefit of ICD implantation by assessing the proportional contribution of SCD to overall mortality.[17] Similarly, the PROFID risk framework represents a contemporary approach that integrates a wide range of clinical and electrocardiographic variables to provide individualized estimates of SCD risk.[18] However, these models primarily focus on overall mortality and SCD risk and were not specifically designed to predict ICD therapies, such as shocks or antitachycardia pacing, which represent the direct clinical manifestations of malignant ventricular arrhythmias. From this perspective, indices reflecting inflammatory and metabolic status, such as the Naples score, may offer complementary prognostic information beyond existing risk models.

Systemic inflammation and immune response are among the key mechanisms that can trigger the arrhythmogenic process. Inflammatory processes may contribute to arrhythmogenic remodeling through myocardial fibrosis, altered ion channel expression, disrupted intercellular communication, and electrical instability.[19] Parameters such as the NLR and LMR are practical markers that reflect such immunological imbalances. Chronic inflammation and poor nutritional status may impair myocardial healing, disrupt sympathovagal balance, and increase susceptibility to arrhythmias. Although this mechanistic framework supports a potential association between the Naples score and arrhythmic risk, the clinical relevance of this relationship appears modest based on the current data. Therefore, although immunonutritional indices such as the Naples score may have potential clinical utility, their adequacy as standalone tools for risk stratification remains uncertain. The Naples score has previously been validated in various clinical settings, including oncology, colorectal surgery, ST-elevation myocardial infarction, and heart failure.[8,9,20,21] By combining serum albumin, total cholesterol, NLR, and LMR, the score provides an overview of a patient's immunonutritional status. Previous studies have linked higher Naples scores to worse cardiovascular outcomes, prolonged hospital stays, and increased mortality. This study investigated whether the Naples score, an index based on inflammation and nutritional status, could predict the risk of ICD shock. Our findings showed that patients who received ICD shocks had significantly higher Naples scores, suggesting that systemic inflammation and nutritional imbalance may contribute to the arrhythmogenic process. However, this association did not remain independent in the multivariable analysis. Accordingly, multivariable logistic regression demonstrated that the Naples score was not an independent predictor of ICD shock. This finding suggests that although the Naples score demonstrates a significant association at the univariable level, it may not be sufficient as an independent predictor when accounting for other strong clinical variables.

ROC analysis demonstrated that the discriminative ability of the Naples score for predicting ICD shocks was limited (AUC: 0.567, 95% CI: 0.506–0.628). Although a statistically significant association was observed ($p = 0.032$), the small difference in median Naples scores between the groups (2 vs. 3) and the AUC value being only marginally above that of random prediction suggest that the Naples score alone is not clinically sufficient as a strong predictor. These findings suggest that the clinical use of the Naples score should be interpreted with caution, as statistical significance does not necessarily translate into clinically meaningful discriminatory performance; therefore, it should not be used as a standalone decision-making tool.

Limitations

This study has several limitations that should be acknowledged. First, its single-center and retrospective design may limit the generalizability of the findings. Second, due to the observational nature of the study, a causal relationship between the Naples score and the occurrence of ICD shocks cannot be established. Third, although multivariable adjustment was performed, residual confounding due to unmeasured or incompletely captured variables cannot be excluded. In addition, the relatively short follow-up duration may have limited the assessment of ICD therapies occurring in the late follow-up period. Finally, although the sample size was moderate, larger prospective multicenter studies involving broader patient populations are needed to validate our findings and enhance statistical power.

Conclusion

The Naples score is a simple and readily accessible index reflecting systemic inflammation, nutritional status, and metabolic status, and may provide potential complementary insight into the biological basis of arrhythmic risk. Since ICD shocks arise from the interplay of multiple factors, including myocardial scar burden, electrophysiological substrate, autonomic balance, and device programming, a single inflammation-based score is unlikely to fully capture this complex process. In the present study, the Naples score was not identified as an independent predictor in multivariable analysis. Accordingly, the clinical use of the Naples score

should be interpreted cautiously and in conjunction with established clinical risk factors. The main advantages of the Naples score include its low cost, ease of calculation, and availability in routine clinical practice. Future prospective and larger-scale studies are needed to better define the potential role of this index when integrated with other clinical and biological parameters.

Author Contributions

Conception and design of the research, writing of the manuscript and critical revision of the manuscript for intellectual content: Sari H, Alsancak Y; acquisition of data: Keskin O; analysis and interpretation of the data and statistical analysis: Sari H, Keskin O.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Necmettin Erbakan University under protocol number 2025/5804. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was not applicable to this study.

Use of Artificial Intelligence

OpenAI's ChatGPT (version GPT-5) to assist with grammar checking and language refinement. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the final text.

Availability of Research Data

All datasets supporting the results of this study are available upon request from the corresponding author.

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