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ORIGINAL RESEARCH

Delta Neutrophil Index in Coronary Artery Bypass Surgery: An Innovation in Postoperative Mortality Assessment

Abdulkadir Bilgiç[1], Burak Toprak[2], Hamide Kaya[3]

[1]Department of Cardiovascular Surgery, Mersin University Faculty of Medicine Hospital, Mersin, Turkey; [2]Department of Cardiovascular Surgery, Mersin City Education and Research Hospital, Mersin, Turkey; [3]Department of Microbiology, Mersin University Faculty of Medicine Hospital, Mersin, Turkey

Correspondence: Burak Toprak, Department of Cardiovascular Surgery, Mersin City Education and Research Hospital, Kuzeykent District, 31131 Street No: 1, Floor: 6, Flat No: 11, Yenişehir, Mersin, 33120, Turkey, Email brk.tprk@gmail.com

Background: Recent interest has focused on the role of inflammatory markers in assessing coronary artery disease (CAD) severity, especially in the early stages. However, there remains a gap in identifying reliable biomarkers to predict postoperative mortality in patients undergoing coronary artery bypass grafting (CABG). Traditional markers such as C-reactive protein (CRP) and white blood cell (WBC) counts are commonly used but have limitations in specificity and prognostic value. The Delta Neutrophil Index (DNI), which reflects immature granulocyte levels, offers a promising alternative. Unlike CRP and WBC, DNI specifically measures the acute inflammatory response, providing a more targeted indicator of risk. This study evaluates the significance of postoperative DNI as a prognostic marker for early mortality in CABG patients, addressing the need for more accurate biomarkers in postoperative care.

Aim: The aim of this study is to determine the significance of the Delta Neutrophil Index (DNI), which reflects the proportion of immature granulocytes, as a prognostic marker for early postoperative mortality in patients undergoing coronary artery bypass grafting (CABG).

Methods: This rigorously designed retrospective cohort study was conducted at a high-volume tertiary care center specializing in cardiovascular surgery, including a robust patient cohort to ensure comprehensive data analysis and reliable conclusions. The study included a consecutive series of 446 patients who underwent coronary artery bypass grafting (CABG) between January 1, 2022, and August 1, 2023.

Results: Mortality was found to be associated with preoperative DNI ($p<0.05$). A 1-unit increase in pre-DNI measurement was associated with a 2.61-fold (95% Confidence Interval: 1.54–4.45) increase in the risk of death. Additionally, mortality was also associated with postoperative DNI ($p<0.05$). A 1-unit increase in postoperative DNI measurement was associated with a 10.21-fold (95% Confidence Interval: 5.08–20.05) increase in the risk of death.

Conclusion: Elevated DNI values are strong independent predictors of postoperative mortality, underscoring its critical role in perioperative risk assessment for CABG patients. Both preoperative and postoperative DNI levels are significantly linked to mortality, emphasizing DNI's value in improving patient outcomes and reducing complications. Integrating DNI into routine clinical practice can provide a more personalized approach to care, enhancing survival and optimizing postoperative management.

Keywords: delta neutrophil index, coronary artery bypass grafting, postoperative mortality, inflammatory markers

Introduction

Coronary artery disease (CAD) is the leading cause of cardiovascular mortality worldwide, resulting in over 4.5 million deaths in developing countries.[1] Coronary artery bypass grafting (CABG) has been shown to improve overall health-related quality of life and survival.[2,3] Outcomes related to cardiac surgery, particularly CABG, have been extensively reported in the United States, Canada, and Western Europe.[4–8] Recently, there has been increasing interest in the role of inflammatory markers in assessing severity early after CABG. CABG leads to an excessive inflammatory response in the postoperative phase.[9] Despite experimental and clinical evidence of the relationship between inflammation and adverse outcomes,[9] no

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specific inflammatory biomarkers are routinely used to predict postoperative mortality in CABG patients. What if we could reliably predict postoperative complications with a simple blood test? The absence of a standardized marker underscores the need for identifying novel prognostic tools to improve postoperative management and patient survival. Immature granulocytes are a practical marker of local and systemic inflammation.[10–12] The use of specific automated blood cell analysis devices allows for the rapid determination of the delta neutrophil index (DNI), which reflects the fraction of circulating immature granulocytes, in conjunction with a complete blood count (CBC).[11,13–15] In this study, we assessed the importance of early postoperative DNI as a prognostic marker for mortality in CABG patients. To our knowledge, this is the first study to evaluate the relationship between DNI and postoperative mortality in a clinical setting.

Methods

This retrospective, observational cohort study was conducted at Mersin University Medical Faculty Training and Research Hospital, a tertiary academic hospital specializing in cardiovascular surgery. The study included consecutive patients who underwent coronary artery bypass grafting (CABG) between January 1, 2022, and August 1, 2023.

Data Collection

Study Design

A nested case-control design within the cohort was employed. When the odds ratio (OR) for delta neutrophil index (DNI) and other factors associated with mortality was set at 1.5 (the minimum clinically significant level), the width of the confidence interval was considered to be 25%. Based on these parameters, the required sample size was determined to be 445. The number of patients who died was matched in a 1:4 ratio to those who survived.

Data Collection

Data on patients' demographics, laboratory test results, operation time, left ventricular ejection fraction (EF), and presence of multi-vessel disease were reviewed. Venous blood samples were collected at admission and postoperatively on a daily basis in vacuum tubes containing ethylenediaminetetraacetic acid (EDTA). Complete blood count (CBC) measurements were performed at multiple time points. Additionally, the duration of cardiopulmonary bypass (CPB) and cross-clamp times were recorded to assess their impact on postoperative mortality and recovery. Although postoperative complications such as stroke, infection, and renal failure were not systematically recorded, the potential relationship between these complications and elevated Delta Neutrophil Index (DNI) levels was considered for future analysis. DNI, white blood cell (WBC) count, hemoglobin level, and platelet count were analyzed by an automated blood cell analyzer.

Data Analysis

Statistical Analysis

For continuous measurements, mean and standard deviation, median, minimum, and maximum values were used. Frequencies and percentages were used for categorical variables. Student's *t*-test was applied for comparisons of age, EF, and biochemical measurements based on mortality status, while paired *t*-test was used for comparing repeated measurements. Chi-Square test was applied to examine the relationship between mortality status and variables such as gender, diabetes mellitus (DM), and hypertension (HT). Odds ratios and 95% confidence intervals were provided for parameters believed to be associated with mortality, including age, gender, EF, DM, HT, and biochemical parameters. Statistical significance was set at $p<0.05$. IBM SPSS 21 and MedCalc statistical software were used for data evaluation. Parametric tests were applied to continuous measurements without normality testing, due to the applicability of the Central Limit Theorem.[16]

Data Availability Statement

Datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Approval

Ethical approval for the study was obtained from the Mersin University Ethics Committee with the decision numbered 2024/472 and dated 22/05/2024.

Declaration of Helsinki

The Study and the Writing of the Article Were Prepared in Accordance With the Declaration of Helsinki.

Informed Written Consent

Informed written consent was obtained in the surgical consent form before the subjects were included in the study.

Results

A total of 446 diagnosed patients were included in the study. The basic characteristics and clinical data are presented in Table 1.

Table 1 Distribution of Socio-Demographic Characteristics in Patients Undergoing Open Heart Vascular Surgery (n=446)

Characteristic	**Mean±SD**	**Median(Min-Mak)**
Age (year)*	64.7±9.8	66(26–85)
	Count (n)	**Percentage (%)**
Gender**		
Male Female	312 134	70 30
DM**		
No Yes	192 254	43 57
HT**		
No Yes	280 166	62,8 37,2
Mortality**		
Alive Exitus	350 96	78,5 21,5
	$(\bar{x} \pm SS)$	**Median (Min-Maks.)**
EF*	52.64±7.09	55(29–65)
PREOP		
Creatinine (mg/dL)*	0.96±0.57	0.88(0.44–9.75)
Urea (mg/dL)*	38.91±15.65	35.6(16.85–114.85)
DNI*	0.48±0.27	0.4(0.10–5.1)
NEU (103mcL)*	5.58±1.34	5.02(1.01–14.95)
LYM (103mcL)*	2.02±0.78	1.94(0.32–5.79)

(*Continued*)

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Table 1 (Continued).

Characteristic	Mean±SD	Median(Min-Mak)
PLT (103mcL)*	238.03±63.03	233(79–519)
CRP (mg/L)*	23.54±18.78	8.89(0.43–413.27)
Albumin (mg/L)*	37.75±3.94	38.32(24.15–46.4)
	Mean±SD	**Min-Max**
CPB Duration (minutes)*	119.49±45.03	112.5 (36–254)
Cross-clamp Duration (minutes)*	70.94±30.01	62.5(12–143)

Notes: *Student's *t*-test, *Chi-Square test (p<0.05 significance), Paired *t*-test, p-value: Student's *t*-test was used for continuous variables, paired *t*-test for repeated measures, and Chi-Square test for categorical variables.

Abbreviations: SD, Standard Deviation; EF, Ejection Fraction; DM, Diabetes Mellitus; HT, Hypertension; CRP, C-Reactive Protein; PLT, Platelets; NEU, Neutrophils; LYM, Lymphocytes; DNI, Delta Neutrophil Index; CPB, Cardiopulmonary Bypass.

According to Table 1, the demographic and clinical characteristics of 446 patients who underwent CABG (Coronary Artery Bypass Grafting) were examined. The age range of the patients was from a minimum of 26 years to a maximum of 85 years, with a mean age of 64.7 ± 9.8 years and a median age of 66 years. Gender distribution showed that 70% of the patients were male, and 30% were female. Diabetes Mellitus (DM) was present in 57% of the patients, while 37.2% had hypertension (HT). The mortality rate was 21.5%, with 350 patients (78.5%) surviving and 96 (21.5%) passing away. The mean Left Ventricular Ejection Fraction (EF) was 52.64 ± 7.09%, with a median of 55%, and EF ranged from 29% to 65% (Table 1).

Preoperative laboratory findings revealed a mean creatinine level of 0.96 ± 0.57 mg/dL, with a median value of 0.88 mg/dL, and urea levels had a mean of 38.91 ± 15.65 mg/dL, with a median value of 35.6 mg/dL. The mean duration of cardiopulmonary bypass (CPB) was 119.49 ± 45.03 minutes, with a median of 112.5 minutes (range: 36–254 minutes). The mean cross-clamp duration was 70.94 ± 30.01 minutes, with a median of 62.5 minutes (range: 12–143 minutes). The Delta Neutrophil Index (DNI) had a mean value of 0.48 ± 0.27, with a median of 0.4, and ranged from 0.10 to 5.1. Neutrophil counts had a mean of 5.58 ± 1.34 × 10^3/μL, with a median value of 5.02 × 10^3/μL, while lymphocyte counts averaged 2.02 ± 0.78 × 10^3/μL, with a median of 1.94 × 10^3/μL. Platelet counts averaged 238.03 ± 63.03 × 10^3/μL, with a median of 233 × 10^3/μL. The mean C-Reactive Protein (CRP) level was 23.54 ± 18.78 mg/L, with a median value of 8.89 mg/L. Finally, albumin levels had a mean of 37.75 ± 3.94 mg/dL, with a median value of 38.32 mg/dL. These findings provide a comprehensive overview of the baseline characteristics and preoperative biochemical measurements in this cohort of CABG patients (Table 1).

In our study, the Delta Neutrophil Index (DNI) was found to be significantly associated with mortality. Patients with elevated DNI levels had a higher risk of postoperative mortality compared to those with lower DNI levels. Particularly in patients undergoing open-heart surgery, elevated preoperative DNI levels indicated an overactive inflammatory response post-surgery, which was associated with an increased mortality rate.

In conclusion, elevated DNI levels were identified as a critical factor contributing to increased mortality risk in surgical patients. Proactive management and closer postoperative monitoring of patients with high DNI values could be essential in reducing mortality rates in this population.

According to Table 2, the relationships between mortality status and socio-demographic and biochemical parameters were evaluated. The difference in average age based on mortality status was not statistically significant (p>0.05). However, gender showed a significant association with mortality (p<0.05). Among deceased patients, 60.4% were male and 39.6% were female, whereas the gender distribution among survivors varied. A significant difference was found in the mean Ejection Fraction (EF) between mortality statuses (p<0.05), with the average EF in deceased patients being 50.26±9.01%, compared to 53.12±6.56% in survivors. A significant relationship was observed between mortality status and the presence of Diabetes Mellitus (DM) (p<0.05). DM was present in 37.75% of deceased patients, whereas the prevalence in survivors was 62.32% (Table 2).

Table 2 Assessment of Differences and Associations in Socio-Demographic and Biochemical Measurements According to Mortality Status (n=446)

		Alive (n=350)	**Exitus (n=96)**	
Features		**Mean±SD**	**Mean±SD**	**p-value*/*** **
Age (year)		63.88±9.52	64.64±12.72	0.52
EF		53.12±6.56	50.26±9.01	**0.01**
Pre-Creatinine (mg/dL)		0.94±0.54	1.1±0.35	0.21
Post-Creatinine (mg/dL)		0.99±0.56	1.35±0.57	**<0.0001**
p value**		**0.002**	**<0.0001**	
Pre-Urea (mg/dL)		38.37±16.96	42.71±13.81	**0.02**
Post-Urea (mg/dL)		36.86±13.71	53.01±23.18	**<0.0001**
p value**		**0.02**	**0.0001**	
Pre-IG		0.42±0.27	0.88±0.63	**0.001**
Post-IG		0.58±0.28	1.66±1.19	**<0.0001**
p value**		**<0.0001**	**<0.0001**	
Pre-NEU (103mcL)		5.56±2.41	5.66±2.66	0.74
Post- NEU (103mcL)		10.03±3.87	12.76±5.18	**<0.0001**
p value**		**<0.0001**	**<0.0001**	
Pre-LYM (103mcL)		2.03±0.68	2.14±1.21	0.43
Post-LYM (103mcL)		1.13±0.48	1.53±1.02	**0.02**
p value**		**<0.0001**	**<0.0001**	
Pre-PLT (103mcL)		237.11±69.32	232.74±75.95	0.6
Post-PLT (103mcL)		156.68±48.83	138.81±71.83	0.06
p value**		**<0.0001**	**<0.0001**	
Pre-CRP (mg/L)		19.06±17.11	26.99±22.39	0.36
Post-CRP (mg/L)		149.32±57.51	134.71±53.34	0.24
p value**		**<0.0001**	**<0.0001**	
Pre-Albumin (mg/L)		38.17±3.47	35.36±5.59	**0.003**
Post-Albumin (mg/L)		28.65±12.55	23.84±4.32	**0.02**
p value**		**<0.0001**	**<0.0001**	
		n(%)	**n(%)**	
Gender	Male Female	254(72.6) 96(27.4)	58(60.4) 38(39.6)	**0.02*****
DM+		218(62.3)	36(37.5)	**<0.0001*****
HT+		136(38.9)	30(31.3)	0.17***

Notes: *Student's *t*-test, **Paired *t*-test, ***Chi-Square test (p<0.05 significance), p-value: Student's *t*-test was used for continuous variables, paired *t*-test for repeated measures, and Chi-Square test for categorical variables. Statistical significance was considered at $p < 0.05$. The values marked in bold in the table indicate statistically significant results.
Abbreviations: EF, Ejection Fraction; DM, Diabetes Mellitus; HT, Hypertension; CRP, C-Reactive Protein; PLT, Platelets; NEU, Neutrophils; LYM, Lymphocytes; DNI, Delta Neutrophil Index; CPB, Cardiopulmonary Bypass.

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Regarding postoperative biochemical parameters, mortality was significantly associated with postoperative creatinine ($p<0.05$), urea ($p<0.05$), neutrophil levels ($p<0.05$), lymphocyte counts ($p<0.05$), Delta Neutrophil Index (DNI) ($p<0.05$), and albumin levels ($p<0.05$).

When examining the preoperative and postoperative biochemical parameters in deceased patients, significant differences were found in creatinine, urea, DNI, neutrophils, lymphocytes, platelets, CRP, and albumin ($p<0.05$). Similarly, in surviving patients, significant differences were observed in creatinine, urea, DNI, neutrophils, lymphocytes, platelets, CRP, and albumin values ($p<0.05$).

These findings suggest significant relationships between mortality and various socio-demographic and biochemical parameters. Notably, left ventricular ejection fraction (EF), diabetes mellitus status, and postoperative biochemical measurements (creatinine, urea, neutrophils, lymphocytes, DNI, and albumin) were critical factors influencing mortality risk.

In conclusion, monitoring these parameters preoperatively and postoperatively may provide essential insights into patient management and outcomes. A proactive approach in managing patients with elevated risk factors could improve clinical outcomes and reduce mortality rates in this population.

According to Table 3, In the evaluation of factors affecting mortality, the analysis revealed that age was not significantly associated with mortality ($p>0.05$). However, a significant relationship was found between mortality and Ejection Fraction (EF) ($p<0.05$). A 1-unit increase in EF reduced the risk of death by 0.95 times (95% Confidence Interval: 0.92–0.98). Mortality was also found to be significantly associated with gender ($p<0.05$), with male patients having a 1.78 times higher likelihood of death compared to female patients (95% Confidence Interval: 1.08–2.78). Additionally, a significant association was observed between mortality and the presence of Diabetes Mellitus (DM) ($p<0.05$). The risk of death was 2.75 times higher in patients with DM (95% Confidence Interval: 1.73–4.39). In contrast, hypertension (HT) did not show a significant relationship with mortality ($p>0.05$) (Table 3).

These findings highlight key factors influencing mortality in patients undergoing coronary bypass surgery. Notably, a low Ejection Fraction (EF) and the presence of diabetes mellitus (DM) significantly increase the risk of death. It is also striking that male patients face a higher mortality risk compared to females. These results emphasize the importance of considering EF and DM in preoperative risk assessments, with gender also being an important factor to take into account. Understanding these associations can inform clinical decision-making and improve patient management strategies in the context of open-heart surgery.

According to Table 4, The analysis of preoperative biochemical parameters revealed significant associations with mortality. Preoperative urea levels were found to be significantly related to mortality ($p<0.05$). A 1-unit increase in preoperative urea raised the risk of death by 1.02 times (95% Confidence Interval: 1.001–1.03). Additionally, the preoperative Delta Neutrophil Index (DNI) was strongly associated with mortality ($p<0.05$). Each 1-unit increase in preoperative DNI increased the risk of death by 2.61 times (95% Confidence Interval: 1.54–4.45). Furthermore, preoperative albumin levels were inversely related to mortality ($p<0.05$), with a 1-unit increase in preoperative albumin reducing the risk of death by 0.84 times (95% Confidence Interval: 0.78–0.92). Other preoperative parameters such as creatinine, neutrophils, lymphocytes, platelets, and C-Reactive Protein (CRP) did not show significant associations with mortality (Table 4).

Table 3 Assessment of the Association Between Mortality and Age, Gender, and Chronic Disease Status (n=446)

Variables	Odds ratio	95% CI	p-value
Age	1.1	0.98–1.03	0.52
Ejection Fraction (EF)	0.95	0.92–0.98	**0.003**
Gender (Risk: Male)	1.73	1.08–2.78	**0.02**
Diabetes Mellitus (DM) (Risk: Present)	2.75	1.73–4.39	**<0.0001**
Hypertension (HT) (Risk: Present)	1.39	0.86–2.26	0.17

Notes: Logistic regression analysis was performed to evaluate the effects on mortality. Statistical significance was considered at $p < 0.05$. The values marked in bold in the table indicate statistically significant results.

Abbreviations: CI, Confidence Interval; EF, Ejection Fraction; DM, Diabetes Mellitus; HT, Hypertension.

Table 4 Assessment of the Association Between Preoperative Biochemical Parameters and Mortality (n=446)

Variables	Odds ratio	95% CI	p-value
Pre-Creatinine (mg/dL)	1.13	0.85–1.51	0.41
Pre-Urea (mg/dL)	1.02	1.001–1.03	**0.03**
Pre-DNI	**2.61**	1.54–4.45	**<0.0001**
Pre-NEU (103mcL)	1.02	0.93–1.11	0.74
Pre-LYM (103mcL)	1.16	0.89–1.52	0.28
Pre-PLT (103mcL)	0.99	0.98–1.01	0.6
Pre-CRP (mg/L)	1.01	0.99–1.001	0.19
Pre-Albumin (mg/L)	−0.84	0.78–0.92	**<0.0001**

Notes: Logistic regression analysis was performed to evaluate the effect of preoperative biochemical parameters on mortality. Statistical significance was considered at $p < 0.05$. The values marked in bold in the table indicate statistically significant results.
Abbreviations: CI, Confidence Interval; DNI, Delta Neutrophil Index; CRP, C-Reactive Protein; NEU, Neutrophils; LYM, Lymphocytes; PLT, Platelets; EF, Ejection Fraction.

These findings highlight the strong association between preoperative Delta Neutrophil Index (DNI) levels and mortality risk. A 1-unit increase in DNI significantly raises the risk of death by 2.61 times, emphasizing its potential as a critical marker in surgical risk assessment. Additionally, higher preoperative urea and lower albumin levels are also linked to mortality, but the impact of DNI is much more pronounced. These results suggest that DNI could serve as a key tool in determining patient risk levels.

Accord'ng to Table 5, The analysis of postoperative biochemical parameters revealed several factors significantly associated with mortality. Postoperative creatinine levels were found to be strongly linked to mortality, with each 1-unit increase in creatinine raising the risk of death by 2.65 times (95% Confidence Interval: 1.5–4.55, $p<0.0001$).

Table 5 Assessment of the Association Between Postoperative Biochemical Parameters and Mortality (n=446)

Variables	Odds ratio	95% CI	p-value
Post-Creatinine (mg/dL)	2.65	1.5–4.55	**<0.0001**
Post-Urea (mg/dL)	1.05	1.03–1.07	**<0.0001**
Post-DNI	**10.21**	5.08–20.5	**<0.0001**
Post- NEU (103mcL)	1.14	1.08–1.21	**<0.0001**
Post-LYM (103mcL)	1.85	1.29–2.64	**0.001**
Post-PLT (103mcL)	0.98	0.97–0.99	**0.02**
Post-CRP (mg/L)	0.99	0.98–1.01	0.25
Post-Albumin (mg/L)	−0.67	0.59–0.76	**<0.0001**

Notes: Logistic regression analysis was performed to evaluate the effect of postoperative biochemical parameters on mortality. Statistical significance was considered at $p < 0.05$. The values marked in bold in the table indicate statistically significant results.
Abbreviations: CI, confidence interval; DNI, Delta Neutrophil Index; CRP, C-Reactive Protein; NEU, Neutrophils; LYM, Lymphocytes; PLT, Platelets; EF, Ejection Fraction.

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Similarly, postoperative urea levels also showed a significant association with mortality; each 1-unit increase in urea raised the risk by 1.05 times (95% Confidence Interval: 1.03–1.07, p<0.0001). Postoperative Delta Neutrophil Index (DNI) exhibited the most striking correlation with mortality, as each 1-unit increase in postoperative DNI increased the risk of death by 10.21 times (95% Confidence Interval: 5.08–20.05, p<0.0001). Additionally, postoperative neutrophil levels were linked to mortality, with each 1-unit increase in neutrophils raising the risk of death by 1.14 times (95% Confidence Interval: 1.08–1.21, p<0.0001). Postoperative lymphocyte levels were also associated with an increased risk of mortality, as each 1-unit increase in lymphocytes raised the risk by 1.85 times (95% Confidence Interval: 1.29–2.64, p<0.001). Finally, postoperative albumin levels were inversely related to mortality; higher albumin levels decreased the risk of death by 0.67 times for each 1-unit increase (95% Confidence Interval: 0.59–0.76, p<0.0001). Postoperative platelet levels were associated with a decrease in mortality risk, as each 1-unit increase in platelets decreased the risk by 0.98 times (95% Confidence Interval: 0.97–0.99, p<0.05). However, postoperative CRP levels showed no significant relationship with mortality (p>0.05). These findings underscore the importance of monitoring postoperative biochemical parameters, particularly DNI, as part of risk assessment in the postoperative period (Table 5).

These results underscore the powerful role of postoperative Delta Neutrophil Index (DNI) in predicting mortality, with each increase in DNI dramatically raising the risk of death by over 10 times. This makes DNI a key marker for assessing patient risk in the postoperative period. Additionally, elevated levels of creatinine, urea, neutrophils, and lymphocytes, as well as low albumin, further contribute to higher mortality, highlighting the importance of comprehensive biochemical monitoring after surgery. However, DNI stands out as the most significant predictor, suggesting it could be a game changer in early risk assessment.

Discussion

In this single-center retrospective study, it was determined that the preoperative and postoperative Delta Neutrophil Index (DNI) is a good predictor of mortality after Coronary Artery Bypass Grafting (CABG). Patients undergoing coronary artery surgical revascularization are exposed to various physiological effects. The CABG surgery, one of the most frequently performed operations since the introduction of the Cardiopulmonary Bypass (CPB) machine, has gained significant attention due to its potential to lead to prolonged ventilator weaning, increased renal dysfunction, stroke, deep sternal infections, and death.[17] In contrast to the traditional inflammatory markers used in previous studies, our findings show that the Delta Neutrophil Index (DNI) has a more direct and significant correlation with postoperative mortality, providing a more accurate risk stratification tool. These outcomes are thought to be largely associated with systemic inflammation caused by CPB machines.[18,19]

However, systemic inflammation that arises after CABG procedures is influenced by many factors beyond CPB machines. Tissue damage and contact of non-endothelial surfaces with blood are known primary triggers of Systemic Inflammatory Response Syndrome (SIRS). Nevertheless, current evidence indicates that the mechanical process of extracorporeal circulation and the CPB itself play an important role.[20]

Using an in vivo acute inflammatory model like bypass surgery allows for a more realistic assessment of genotype function compared to in vitro experiments and may reflect clinically significant changes. Similarly, our study confirms that the Delta Neutrophil Index (DNI), which reflects an inflammatory response, is a powerful predictor of postoperative mortality in CABG patients, far surpassing traditional markers like CRP and WBC counts. Neutrophils are critical cells in innate immunity and mediate tissue damage following ischemia-reperfusion injury.[21] Patients in the high DNI group demonstrated worse postoperative outcomes compared to those in the low DNI group. Given the significant relationship between inflammatory responses and postoperative outcomes in cardiac surgery, an objective inflammatory index has been developed to improve risk stratification in cardiac surgery.[22] DNI may represent the degree of inflammation and physical stress caused by surgical stimulation, serving as a valuable prognostic indicator in surgical patients. Our findings corroborate this hypothesis, as elevated DNI levels were significantly associated with increased mortality rates, highlighting its relevance not only in assessing surgical stress but also in guiding postoperative patient management. Moreover, our study expands on existing research by demonstrating that both preoperative and postoperative DNI levels consistently correlate with mortality, which supports the use of DNI as a key marker for continuous patient monitoring

after surgery. Given its predictive power, the incorporation of DNI into existing risk models could revolutionize patient monitoring protocols, enabling earlier interventions and reducing the burden of postoperative complications. Future research should focus on integrating DNI into comprehensive risk models that incorporate both inflammatory and hemodynamic parameters for enhanced predictive accuracy. Therefore, we assessed the impact of DNI on outcomes after CABG. In the present study, mortality was associated with Pre-IG ($p<0.05$). A 1-unit increase in Pre-IG measurement increased the risk of death by 2.61 (95% CI: 1.54–4.45). Mortality was also associated with Post-IG ($p<0.05$). A 1-unit increase in Post-IG measurement increased the risk of death by 10.21 (95% CI: 5.08–20.05). Notably, preoperative and postoperative DNI showed significant relationships with mortality. These findings suggest that measuring pre-DNI and post-DNI together may be useful for better risk classification and screening of high-risk patients.

However, these are not definitive diagnostic markers and should be used alongside other clinical evaluations. DNI was significantly associated with well-known risk factors for poor prognosis after cardiac surgery, indicating that DNI may be influenced by the patient's underlying condition and that it can accurately represent this.

Previous studies reported that the inflammatory response after cardiac surgery peaks within 48 hours and shows a tendency to decrease.[23,24] In contrast, our study highlights the significant predictive value of both preoperative and postoperative DNI, which continued to show strong associations with mortality beyond the 48-hour mark, emphasizing its utility in extended postoperative monitoring. DNI may be a valuable indicator in identifying patients who are not in the high-risk group preoperatively but have a poor recovery process postoperatively. In this context, the current study observed a higher incidence of postoperative hospital morbidity in the high DNI group compared to the low DNI group.

Consistent with the results of this study, the benefit of the Delta Neutrophil Index in predicting 30-day mortality in patients with ST-segment elevation myocardial infarction has been demonstrated.[25] Additionally, in terms of sepsis, Park et al revealed that DNI >6.5% within the first 24 hours after admission to the intensive care unit is a good diagnostic marker for severe sepsis and septic shock.[10] Similarly, our findings demonstrate that a higher DNI, both pre- and postoperatively, significantly correlates with mortality in CABG patients, suggesting that DNI can serve as a crucial early marker for predicting adverse outcomes in a broader surgical context. Previous studies have proposed potential mechanisms to explain the rapid and early release of immature granulocytes. In cases of sterile inflammation, such as OPCAB, the mechanism of increasing immature granulocytes likely resembles that in sepsis. For example, in severe inflammation, the large consumption and destruction of mature cells may lead to a rapid expansion of circulating neutrophils to compensate for the loss of active neutrophils.[26–30] This mechanism aligns with our observation that patients with higher DNI levels exhibited worse outcomes, suggesting that DNI could be a useful marker for detecting heightened inflammatory responses that contribute to mortality after CABG Our study extends this concept by showing that elevated DNI levels in CABG patients, reflective of heightened granulocyte production, are strongly predictive of mortality, reinforcing the importance of managing inflammatory responses in the postoperative period. Moreover, in myocardial reperfusion injury, reperfusion causes endothelial dysfunction, leading to vasoconstriction within the first few minutes, while increased leukocyte adhesion and flow contribute to impaired blood flow.[31] This could be a promising biomarker for predicting postoperative DNI mortality after reperfusion. Building on this, our results confirm that postoperative DNI is a robust predictor of mortality following CABG, particularly in patients undergoing reperfusion, suggesting its potential integration into routine postoperative risk assessments.

While previous studies primarily examined long-term outcomes, our study focuses solely on short-term mortality and postoperative complications, providing strong evidence for DNI's effectiveness as an early predictor of these outcomes. While CRP, WBC, and Neutrophil levels significantly increased in patients after surgery, DNI levels remained within normal ranges in survivors. These findings clearly demonstrate the activation of opposing immune-inflammatory pathways induced by CABG and confirm the importance of DNI as a risk stratification marker.

To our knowledge, this is the first study to directly investigate the relationship between Delta Neutrophil Index (DNI) and postoperative mortality in patients undergoing coronary artery bypass grafting (CABG). While previous studies have explored the role of inflammatory markers such as C-reactive protein (CRP) and white blood cell (WBC) counts in CABG outcomes, none have specifically focused on DNI as a prognostic tool. Therefore, the findings of this study are unique in demonstrating the potential of DNI to serve as an early indicator of mortality risk in CABG patients, highlighting its distinct value compared to other traditional markers.

Conclusions

In conclusion, the increased Delta Neutrophil Index (DNI) value, reflecting the proportion of circulating immature granulocytes in the blood, has been found to be an independent predictor of postoperative mortality and poor clinical outcomes following Coronary Artery Bypass Grafting (CABG). Both preoperative and postoperative DNI were significantly associated with mortality, indicating the valuable roles of DNI in the risk assessment necessary for perioperative and postoperative management. This highlights the dual utility of DNI in not only predicting but also monitoring patient outcomes throughout the perioperative period.

As a secondary outcome, DNI may serve as a valuable indicator for identifying patients who are not in the high-risk group according to current risk assessment scores but have a poor recovery process postoperatively, potentially leading to increased morbidity and mortality risk.

Limitations of the Study

This study has several potential limitations. Despite encompassing a relatively large patient cohort, the nature of its single-center observational retrospective design imposes certain constraints. This design has limited the ability to perform meaningful subgroup analyses and has restricted the examination of subgroups such as patients with heart failure, those with high EuroSCORE, and those requiring urgent or reoperation. Therefore, broader-scale studies including such high-risk patient groups are needed.

The study did not identify the underlying pathophysiology of the relationship between Delta Neutrophil Index (DNI) and early complications in adult cardiac surgery. We aimed to minimize bias by using multivariate logistic regression analysis to account for variables that could affect cardiac surgeries performed with Cardiopulmonary Bypass (CPB) and early clinical outcomes. We attempted to mitigate inter-center variability by grouping patients operated on by the same experienced surgical team using the same technique.

Additionally, we evaluated deaths based on general causes without an in-depth analysis of the specific reasons for mortality. Larger-scale randomized controlled trials are needed to validate whether Delta Neutrophil Index is a simple and effective marker in clinical practice and to determine if it impacts clinical outcomes. Although the study is limited by its single-center design, the findings offer a robust foundation for future multicenter, randomized trials aimed at validating DNI as a critical component in perioperative management protocols.

Key Points

a. **What is known about the topic?**

It is well-established that inflammatory responses play a significant role in the outcomes of cardiac surgeries, including coronary artery bypass grafting (CABG). Various inflammatory markers, such as C-reactive protein (CRP) and white blood cell (WBC) counts, have been studied in relation to postoperative outcomes. However, no specific inflammatory biomarker is routinely used in clinical practice to predict postoperative mortality in CABG patients. The delta neutrophil index (DNI), which measures the proportion of immature granulocytes, has been suggested in recent studies as a promising marker for inflammation and may serve as an indicator of poor prognosis in critically ill patients, but its use in CABG remains underexplored.

b. **What does this study add?**

This study introduces the delta neutrophil index (DNI) as a novel prognostic marker for predicting early postoperative mortality in patients undergoing coronary artery bypass grafting (CABG). It provides the first clinical evidence that both preoperative and postoperative DNI values are significantly associated with increased mortality risk. The findings suggest that DNI could be a valuable tool for risk stratification, enabling more precise perioperative and postoperative management of CABG patients, particularly in identifying those at higher risk for poor outcomes who may otherwise go unnoticed using traditional markers.

Statement on the Use of Artificial Intelligence

No artificial intelligence application was used.

Abbreviations

CABG, Coronary Artery Bypass Grafting; CAD, Coronary Artery Disease; CBC, Complete Blood Count; CRP, C-Reactive Protein; DNI, Delta Neutrophil Index; DM, Diabetes Mellitus; EF, Ejection Fraction; HT, Hypertension; IG, Immature Granulocytes; PLT, Platelets; WBC, White Blood Cell.

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Author Contributions

All authors have made significant contributions to the work reported, which may include the conception, study design, execution, acquisition of data, analysis and interpretation, or all of these areas; drafting, revising, or critically reviewing the article; giving final approval of the version to be published; agreeing on the journal to which the article has been submitted; and accepting responsibility for all aspects of the work.

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References

1. Okrainec K, Banerjee DK, Eisenberg MJ. Coronary artery disease in the developing world. *Am Heart J*. 2004;148:7–15. doi:10.1016/j.ahj.2003.12.029
2. Rumsfeld JS, Magid DJ, O'Brien M, McCarthy M, MaWhinney S, Shroyer AL. Changes in health-related quality of life following coronary artery bypass graft surgery. *Ann Thorac Surg*. 2001;72:2026–2032. doi:10.1016/s0003-4975(01)03150-3
3. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961–972. doi:10.1056/NEJMoa0804626
4. Shroyer AL, Coombs LP, Peterson ED, et al. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. *Ann Thorac Surg*. 2003;75:1856–1864. doi:10.1016/s0003-4975(03)00256-9
5. Agabiti N, Ancona C, Forastiere F, Arca M, Perucci CA. Evaluating outcomes of hospital care following coronary artery bypass surgery in Rome, Italy. *Eur J Cardiothorac Surg*. 2003;23:599–607. doi:10.1016/s1010-7940(03)00041-7
6. Tu JV, Naylor CD. Coronary artery bypass mortality rates in Ontario: a Canadian approach to quality assurance in cardiac surgery. *Circulation*. 1996;94:2429–2433. doi:10.1161/01.cir.94.10.2429
7. Ferguson TB, Hammill BG, Peterson ED, DeLong ER, Grover FL. A decade of change–risk profiles and outcomes for isolated coronary artery bypass grafting procedures 1990–1999: a report from the STS National Database Committee and the Duke Clinical Research Institute. *Ann Thorac Surg*. 2002;73:480–489. doi:10.1016/s0003-4975(01)03338-7
8. Hannan EL, Zhong Y, Lahey SJ, et al. 30-day readmissions after coronary artery bypass graft surgery in New York State. *JACC Cardiovasc Interv*. 2011;4:569–576. doi:10.1016/j.jcin.2011.02.012
9. Brull DJ, Montgomery HE, Sanders J, et al. Interleukin-6 gene −174G>C and −572G>C promoter polymorphisms are strong predictors of plasma interleukin-6 levels after coronary artery bypass surgery. *Arterioscler Thromb Vasc Biol*. 2001;21:1458–1463. doi:10.1161/hq0901.093394
10. Park BH, Kwon J, Lee J. Delta neutrophil index as an early marker of disease severity in critically ill patients with sepsis. *BMC Infect Dis*. 2011;11:299. doi:10.1186/1471-2334-11-299
11. Yune HY, Kim YH, Lee YH. Delta neutrophil index as a promising prognostic marker in out-of-hospital cardiac arrest. *PLoS One*. 2015;10:e0120677. doi:10.1371/journal.pone.0120677
12. Kim OH, Kim YH, Ryu HJ, et al. The use of delta neutrophil index and myeloperoxidase index for predicting acute complicated appendicitis in children. *PLoS One*. 2016;11:e0148799. doi:10.1371/journal.pone.0148799
13. Kim H, Lee JH, Kim JS, et al. Usefulness of the delta neutrophil index as a prognostic marker of acute cholangitis in emergency departments. *Shock*. 2017;47:303–312. doi:10.1097/shk.0000000000000732
14. Ko DR, Lee J, Kim H, et al. Usefulness of the delta neutrophil index as an ancillary test in the emergency department for the early diagnosis of suspected acute promyelocytic leukemia. *Leuk Lymphoma*. 2017;58:1–8. doi:10.1080/10428194.2017.1310047

15. Nahm CH, Choi JW, Lee J. Delta neutrophil index in automated immature granulocyte counts for assessing disease severity of patients with sepsis. *Ann Clin Lab Sci*. 2008;38:241–246.
16. Norman G. Likert scales, levels of measurement and the "laws" of statistics. *Adv Health Sci Educ Theory Pract*. 2010;15:625–632. doi:10.1007/s10459-010-9222-y
17. Shahian DM, O'Brien SM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1--coronary artery bypass grafting surgery. *Ann Thorac Surg*. 2009;88:S2–22. doi:10.1016/j.athoracsur.2009.05.055
18. Brewer R, Theurer PF, Cogan CM, Bell GF, Prager RL, Paone G. Morbidity but not mortality is decreased after off-pump coronary artery bypass surgery. *Ann Thorac Surg*. 2014;97:831–836. doi:10.1016/j.athoracsur.2013.11.059
19. Bicer M, Senturk T, Yanar M, et al. Effects of off-pump versus on-pump coronary artery bypass grafting: apoptosis, inflammation and oxidative stress. *Heart Surg Forum*. 2014;17:E271–276. doi:10.1532/hsf98.2013314
20. Whitten CW, Hill GE, Ivy R, Greilich PE, Lipton JM. Does the duration of cardiopulmonary bypass or aortic cross-clamp, in the absence of blood and/or blood product administration, influence the IL-6 response to cardiac surgery? *Anesth Analg*. 1998;86:28–33. doi:10.1213/00000539-199801000-00006
21. Fang L, Moore XL, Dart AM, Wang LM. Systemic inflammatory response following acute myocardial infarction. *J Geriatr Cardiol*. 2015;12:305–312. doi:10.11909/j.issn.1671-5411.2015.03.024
22. Laffey JG, Boylan JF, Cheng DC. The systemic inflammatory response to cardiac surgery: implications for the anesthesiologist. *Anesthesiology*. 2002;97:215–252. doi:10.1097/00000542-200207000-00031
23. Boyle EM, Pohlman TH, Johnson MC, Verrier ED. Endothelial cell injury in cardiovascular surgery: the systemic inflammatory response. *Ann Thorac Surg*. 1997;63:277–284. doi:10.1016/s0003-4975(97)00025-7
24. Chew MS, Brandslund I, Brix-Christensen V, et al. Tissue injury and the inflammatory response to pediatric cardiac surgery with cardiopulmonary bypass: a descriptive study. *Anesthesiology*. 2001;94:745–753. doi:10.1097/00000542-200105000-00010
25. Kong T, Kim TH, Park YS, et al. Usefulness of the delta neutrophil index to predict 30-day mortality in patients with ST-segment elevation myocardial infarction. *Sci Rep*. 2017;7:15718. doi:10.1038/s41598-017-15718-0
26. Hwang YJ, Ahn KJ, Lee JW, Kim SH, Na MJ. Newly designed delta neutrophil index-to-serum albumin ratio prognosis of early mortality in severe sepsis. *Am J Emerg Med*. 2015;33:1577–1582. doi:10.1016/j.ajem.2015.07.056
27. Bermejo-Martin JF, Almansa R, Torres A, et al. Defining immunological dysfunction in sepsis: a requisite tool for precision medicine. *J Infect*. 2016;72:525–536. doi:10.1016/j.jinf.2016.02.010
28. Alves-Filho JC, Spiller F, Cunha FQ. Neutrophil paralysis in sepsis. *Shock*. 2010;34:15–21. doi:10.1097/shk.0b013e3181e7e61b
29. Leliefeld PH, Wessels CM, Leenen LP, Koenderman L, Pillay J. The role of neutrophils in immune dysfunction during severe inflammation. *Crit Care*. 2016;20:73. doi:10.1186/s13054-016-1235-4
30. Kong T, Lee J, Kim H, et al. Usefulness of the Delta Neutrophil Index to Predict 30-day Mortality in Patients with Upper Gastrointestinal Bleeding. *Shock*. 2017;47:1–8. doi:10.1097/shk.0000000000000756
31. Arslan F, de Kleijn DP, Pasterkamp G. Innate immune signaling in cardiac ischemia. *Nat Rev Cardiol*. 2011;8:292–300. doi:10.1038/nrcardio.2011.38