

Investigation of the effects of preoperative nutritional status scores on renal injury after cardiac surgery in elderly patients

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Abstract. – OBJECTIVE: Acute kidney injury (AKI) is a common complication after cardiac operations accompanied by cardiopulmonary bypass (CPB). Nutritional status is an important parameter that reflects the general health status of patients, and its prognostic importance has been shown in numerous diseases. For this reason, various scoring systems are used to show nutritional status, the most known of which are the controlling nutritional status (CONUT) score and the geriatric nutritional risk index (GNRI). In this current study, we aimed to investigate the prognostic values of the CONUT score and GNRI in predicting AKI after cardiac surgery.

PATIENTS AND METHODS: Patients over sixty-five years of age who underwent cardiac surgery with CPB in our clinic between March 2019 and January 2021, were consecutively included in the study. The patients who did not develop AKI in the postoperative period were recorded as Group 1, whereas the patients who did develop were defined as Group 2.

RESULTS: Postoperative AKI occurred in 126 (28.7%) patients (Group 2). The median age of the 313 patients included in Group 1 and 126 patients in Group 2 was 69 (67 to 81) and 71 (66 to 85) years, respectively ($p = 0.033$). The two groups were similar in terms of gender, body mass index, hypertension, smoking, and left ventricular ejection fraction rates. In Group 2, albumin and GNRI values were significantly lower ($p = 0.019$ and $p < 0.001$, respectively), whereas the CONUT score was significantly higher ($p < 0.001$).

CONCLUSIONS: We showed the CONUT score and GNRI values calculated in the preoperative period in patients over 65 years of age as independent predictors of the development of AKI, after cardiac surgery.

Key Words:

Cardiac surgery, Nutritional status, Elderly patients, Acute kidney injury, Postoperative term.

Introduction

Acute kidney injury (AKI) is a common complication after cardiac operations accompanied by cardiopulmonary bypass (CPB). It occurs at rates of up to 30% in current evaluations, and hemodialysis is required in 2.2% of these patients, in the postoperative period¹. This situation prolongs hospital stays and increases treatment costs. The development of AKI is a multifactorial condition where ischemia-reperfusion injury, oxidative stress states, and inflammation play an important role².

Nutritional status is an important parameter that reflects the general health status of patients and its prognostic importance has been shown in numerous diseases³. It should be noted that malnutrition can be understood from the weight and appearance of patients, as well as the fact that malnutrition may occur in obese individuals⁴. For this reason, various scoring systems are used to show nutritional status, the most known of which are the controlling nutritional status (CONUT) score and the geriatric nutritional risk index (GNRI)^{5,6}. These scoring systems are notably used in the clinical follow-up of the nutritional status of elderly patients. A study⁷ conducted on patients who underwent isolated coronary bypass graft surgery (CABG) showed a significant relationship between the CONUT score and the development of postoperative renal problems. In another recent study⁸, the CONUT score and GNRI values were shown as independent predictors of the development of contrast nephropathy in elderly patients who underwent coronary angiography.

In this current study, we aimed to investigate the prognostic values of the CONUT score and GNRI in predicting AKI after cardiac surgery.

Patients and Methods

Patients over sixty-five years of age who underwent cardiac surgery with CPB in our clinic between March 2019 and January 2021, were consecutively included in the study, which was initiated after the approval of the local ethics committee and conducted in accordance with the Helsinki Declaration. Written informed consent was obtained from all patients before their surgeries. Emergency operations, patients with renal failure in the preoperative period (creatinine >1.5mg/dl), patients with preoperative hemoglobin value <11 g/dL, patients who were reoperated for reasons such as re-operations, bleeding, or preoperative myocardial infarction, patients with critical preoperative condition (those operated under an intra-aortic balloon pump or inotropic support), were excluded from the study. As a result of the exclusion criteria, 439 patients were included in the study.

The data of the study group were obtained from the hospital data recording systems and the intensive care daily follow-up cards. Preoperative characteristics (age, sex, smoking, hypertension, diabetes mellitus, hemogram values, urea, creatinine, CONUT score, GNRI, etc.), the operative data (CBP and cross-clamp times, types of operation, etc.) and the postoperative data (total blood product usage amounts, hospital, intensive care hospital stay, blood values of renal functions, etc.) were all recorded.

Defining Postoperative Renal Insufficiency

Hemograms and biochemical measurements were performed from blood samples taken from all patients three days after the operation. As a result of the evaluations made from these blood parameters, the development of AKI was determined as the primary endpoint of the study. Postoperative AKI assessment was performed according to the kidney disease improving global outcomes (KDIGO) criteria. Accordingly⁹:

Stage 1: An increase of ≥ 0.3 mg/dl in creatinine from baseline or an increase of 1.5 to 1.9 times the initial value

Stage 2: 2.0 - 2.9 times the basal creatinine value,

Stage 3: More than 3-fold increase from baseline or ≥ 4.0 mg/dl increase in serum creatinine or need for renal replacement therapy

The development of one of the above conditions after surgical operations was defined as AKI. As a result of this evaluation, the patients who did not develop AKI in the postoperative period were re-

corded as Group 1, whereas the patients who did develop were defined as Group 2.

Calculation of Nutrition Scores

The blood parameters of the patients were measured from the blood samples obtained from the peripheral venous structures in the preoperative period. Hemogram and biochemical measurements were made on automatic analyzers. The CONUT score is obtained by giving scores according to serum albumin, total lymphocyte count, and cholesterol values. According to this calculation, 0-1 is considered normal, 2-4 mild, 5-8 moderate, and 9-12 severe malnutrition¹⁰.

GNRI = $[1.489 \times \text{albumin (g/L)}] + [41.7 \times (\text{current body weight [kg]} / \text{ideal body weight [kg]})]$ calculated with the formula. In our study, the ideal body weight was calculated with the Lorenz formula⁶.

Males = $\text{height (cm)} - 100 - ((\text{height (cm)} - 150) / 4)$
Females = $\text{height (cm)} - 100 - ((\text{height (cm)} - 150) / 2.5)$

Statistical Analysis

Data analysis was performed using the SPSS 21.0 (IBM Corp., Armonk, NY, USA) program. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to evaluate normality distribution. While student's *t*-test (data expressed as mean \pm sd) was used in the analysis of the data that fit the normal distribution, the Mann-Whitney U test (data expressed as median, minimum-maximum) was used for the analysis of the data that was not normally distributed. Frequency and percentile analysis was performed for nominal data and the Chi-Square test was utilized for comparison. A univariate and multivariate logistic regression analysis was performed to analyze the factors affecting the development of postoperative AKI. The univariate logistic regression analysis was utilized initially, then variables associated with a *p*-value ≤ 0.20 in univariate analyses were considered for inclusion in the multivariate analyses. Multivariate logistic regression analyses Model 1 with CONUT score and Model 2 with GNRI were applied. Receiver operating characteristic (ROC) curve analysis was utilized to determine the cut-off values of the CONUT score and GNRI. Area Under Curves (AUCs) were calculated. A *p*-value of $< .05$ was considered significant.

Table I. Demographic data and preoperative laboratory variables of the patients.

Variables	Group 1 N = 313	Group 2 N = 126	p-value
Age (years)	69 (67-81)	71 (66-85)	0.033
Female gender, n (%)	65 (20.8%)	33 (26.2%)	0.217
Diabetes Mellitus, n (%)	79 (25.2%)	46 (36.5%)	0.018
Hypertension, n (%)	224 (71.6%)	87 (69%)	0.600
BMI, kg/m ²	26.7 ± 2.9	27.5 ± 3.5	0.198
Current Smoker, n (%)	185 (59.1%)	71 (56.3%)	0.596
Hyperlipidemia, n (%)	188 (60.1%)	69 (54.8%)	0.308
Ejection fraction (%)	50 (30-60)	45 (35-65)	0.184
ASA use, n (%)	215 (68.7%)	82 (65.1%)	0.464
ACEI/ ARB use, n (%)	223 (71.2%)	93 (73.8%)	0.588
White blood cell (10 ³ /μL)	7.8 (4.9-12.5)	7.6 (4.2-13.7)	0.276
Hemoglobin (mg/dl)	12.5 (11.6-15.4)	12.2 (11.2-16.1)	0.192
Platelet (10 ³ /μL)	259 (196-377)	261 (185-351)	0.318
Neutrophil (10 ³ /μL)	3.6 (1.5-7.7)	3.8 (1.4-6.8)	0.127
Lymphocyte(10 ³ /μL)	1.5 (0.8-3.9)	1.3 (0.9-3.5)	0.164
Albumin (g/L)	33.2 (29.4-36.8)	30.4 (27.5-35)	0.019
Creatinine (mg/dL)	0.8 (0.6-1.35)	1.2 (0.9-1.46)	< 0.001
BUN (mg/dL)	12 (8-27)	14 (7-25)	0.241
CRP (mg/dL)	7.8 (2.4-25.3)	8.1 (1.7-21.9)	0.347
CONUT score	3 (1-8)	5 (1-8)	< 0.001
GNRI	96.9 (90.4-104)	91.8 (85.4-98)	< 0.001

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid; BMI, body mass index, BUN: Blood urea nitrogen, CRP: C reactive protein, CONUT: Controlling nutritional status, GNRI: Geriatric nutritional risk index.

Results

Postoperative AKI occurred in 126 (28.7%) patients (Group 2). The median age of the 313 patients included in Group 1 and 126 patients in Group 2 was 69 (67 to 81) and 71 (66 to 85) years, respectively ($p = 0.033$). The two groups were similar in terms of hypertension, smoking, gender, body mass index, and left ventricular ejection fraction rates. The rate of diabetes mellitus upon admission to the hospital was higher in Group 2 ($p = 0.018$) (Table I).

There was no significant difference between the groups in terms of white blood cells, hemoglobin, platelet, neutrophil, lymphocyte, urea, and C-reactive protein values. In Group 2, albumin and GNRI values were significantly lower ($p = 0.019$ and $p < 0.001$, respectively), whereas the CONUT score was significantly higher ($p < 0.001$) (Table I).

The operative and postoperative features of the patients are presented in Table II. Cross-clamp times, types of surgeries, and intensive care unit stays were similar between the two groups. Total

Table II. Operative and postoperative features of the patients.

Variables	Group 1 N = 313	Group 2 N = 126	p-value
Total perfusion time	96 (89-199)	107 (92-216)	< 0.001
Cross-clamp time	72 (65-155)	75 (68-148)	0.117
Packed blood products (units)	5 (4-8)	7 (5-11)	< 0.001
Inotropic support, n (%)	33 (10.5%)	25 (19.8%)	0.009
Type of surgery			0.138
Isolated CABG	198	89	
CABG+ valve	75	22	
Isolated valve	25	5	
Double valve	10	5	
Valve+ aortic	5	5	
Total ICU stay (days)	2 (1-9)	2 (1-12)	0.294
Total hospital stay (days)	7 (6-15)	9 (8-27)	< 0.001

ICU: Intensive care unit, CABG: Coronary artery bypass graft.

perfusion time, used packed blood product units, need for inotropic support, and total hospital stay days were statistically significantly higher in Group 2 ($p < 0.001$, $p < 0.001$, $p = 0.009$, and $p < 0.001$, respectively).

In the univariate analysis, AKI was found to significantly correlate with age (odds ratio [OR]: 0.694, 95% confidence interval [CI]: 0.590-0.817, $p = 0.038$), diabetes mellitus (OR: 0.789, 95% CI: 0.647-0.928, $p = 0.026$), total perfusion time (OR: 1.324, 95% CI: 1.090-1.935, $p < 0.001$), blood product use (OR: 0.894, 95% CI: 0.690-0.959, $p < 0.001$), preoperative creatinine value (OR: 2.654, 95% CI: 1.984-3.816, $p < 0.001$), CONUT score > 4 (OR: 2.884, 95% CI: 1.698-4.161, $p < 0.001$) and GNRI (OR: 1.266, 95% CI: 1.080-1.842, $p < 0.001$). In the multivariate analysis Model 1, total perfusion time (OR: 0.895, 95% CI: 0.680-0.972, $p = 0.016$), blood product use (OR: 0.678, 95% CI: 0.554-0.894, $p = 0.026$), preoperative creatinine value (OR: 1.835, 95% CI: 1.546-2.734, $p = 0.009$) and CONUT score > 4 (OR: 1.942, 95% CI: 1.150-2.874, $p = 0.002$) were determined as independent predictors for AKI. In Model 2, total perfusion time (OR: 1.190, 95% CI: 1.070-1.579, $p = 0.009$), need of inotropic support (OR: 1.116, 95% CI: 1.050-1.465, $p = 0.036$), blood product use (OR: 0.796, 95% CI: 0.680-0.912, $p = 0.008$), preoperative creatinine value (OR: 2.138, 95% CI: 1.886-

3.560, $p = 0.002$), and GNRI (OR: 1.120, 95% CI: 1.096-2.116, $p = 0.014$) were determined as independent predictors for AKI (Table III).

Receiver operation characteristic curve analysis was utilized to analyze CONUT score and GNRI in predicting AKI after cardiac surgery. The cut-off value of CONUT score was 3.5 (area under the curve: 0.827, 95% confidence interval: 0.778-0.875, $p < 0.001$, with 86.5% sensitivity and 69% specificity (Figure 1A), and GNRI was 93.6 (area under the curve: 0.710, 95% confidence interval: 0.656-0.774, $p < 0.001$, with 61.7% sensitivity, 55.8% specificity (Figure 1B).

Discussion

Open cardiac surgery is successfully performed in the treatment of many cardiac diseases, particularly coronary artery disease and heart valve diseases. Despite various technical developments, most of these surgeries are today performed with CPB which includes various risks and one of the most important of these is the development of AKI. High preoperative creatinine, increased blood product, use of vasoactive agents, and prolonged CPB, are known risk factors for AKI¹¹. In the current study, we investigated the predictive significance of two nutritional scores after cardiac surgery, in patients over 65 years of age. At the

Table III. Logistic regression analysis to identify factors affecting postoperative acute kidney injury.

Variables	Univariate analysis			Multivariate analysis		
	<i>p</i>	Exp(B) Odds Ratio	95% C.I Lower Upper	<i>p</i>	Exp(B) Odds Ratio	95% C.I Lower Upper
Age	0.038	0.694	0.590-0.817	--	--	--
Diabetes mellitus	0.026	0.789	0.647-0.928	--	--	--
Total perfusion time	< 0.001	1.324	1.090-1.935	0.016 ^a	0.895 ^a	0.680-0.972 ^a
Cross-clamp time	0.126	1.448	0.914-1.672	0.009 ^b	1.190 ^b	1.070-1.579 ^b
Type of surgery	0.146	1.659	0.839-2.116	--	--	--
Inotropic support	0.013	1.420	1.114-1.870	0.056 ^a	1.885 ^a	1.394-2.195 ^a
Blood product use	< 0.001	0.894	0.690-0.959	0.036 ^b	1.116 ^b	1.050-1.465 ^b
Creatinine	< 0.001	2.654	1.984-3.816	0.026 ^a	0.678 ^a	0.554-0.894 ^a
Albumin	0.025	0.572	0.390-0.716	0.008 ^b	0.796 ^b	0.680-0.912 ^b
Lymphocyte count	0.178	0.990	0.754-1.090	0.009 ^a	1.835 ^a	1.546-2.734 ^a
CONUT score > 4	< 0.001	2.884	1.698-4.161	0.002 ^b	2.138 ^b	1.886-3.560 ^b
GNRI	< 0.001	1.266	1.080-1.842	0.002 ^a	1.942 ^a	1.150-2.874 ^a
				0.014 ^b	1.120 ^b	1.096-2.116 ^b

CONUT: Controlling nutritional status, GNRI: Geriatric nutritional risk index, ^aMultivariate analysis Model 1, ^bMultivariate analysis Model 2.

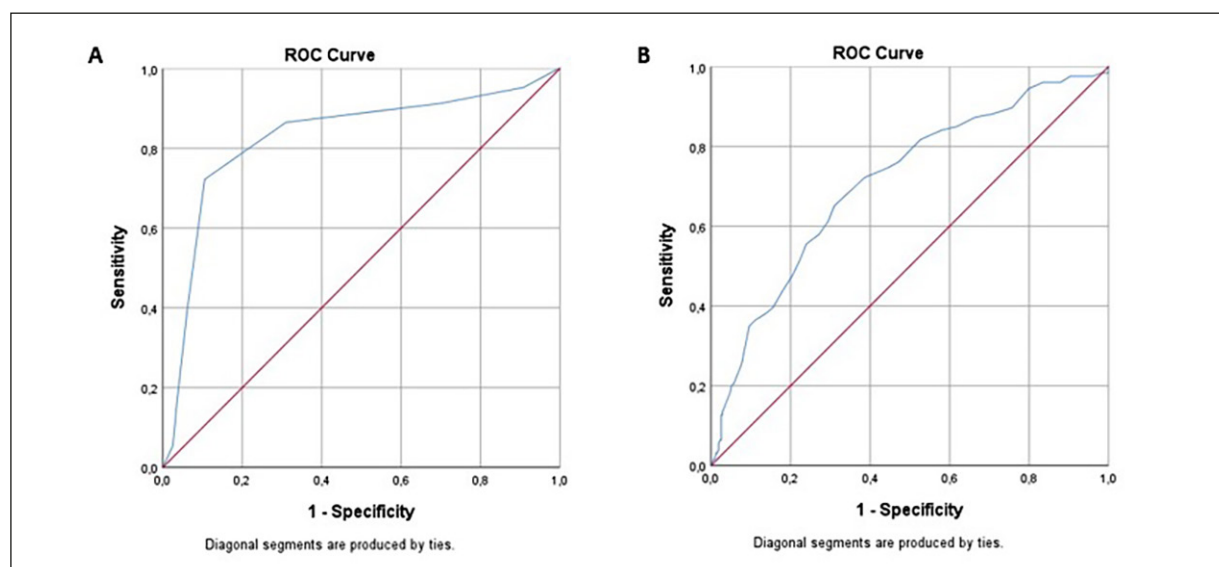


Figure 1. Data figure of the area under the curve (AUC), confidence interval (CI), and cut-off values in receiver-operating characteristic (ROC) curve analysis for (A) CONUT score (cut off: 3.5, AUC: 0.827, 95% CI: 0.778-0.875, $p < 0.001$, with 86.5% sensitivity and 69% specificity) and (B) GNRI (cut off: 93.6, AUC: 0.710, 95% CI: 0.656-0.774, $p < 0.001$, with 61.7% sensitivity and 55.8% specificity) to predict acute kidney injury after cardiac surgery.

outcome, we showed CONUT score and GNRI values as independent predictors of postoperative AKI development, in addition to known risk factors such as increased CPB duration, preoperative creatinine elevation, and blood product use.

In the human body, muscle proteins and albumin are the main sources of essential amino acids. In case of malnutrition, these valuable proteins will be consumed since the energy source will be provided by gluconeogenesis. In addition, regular intake of low-essential amino acids, regardless of calorie intake, can create a permanent consumption situation in the body. In this way, malnutrition may reduce the efficiency of the pancreas and mesenteric circulation, and amino acid absorption may be impaired¹². In this respect, albumin is a very important protein for the body, but it also plays an important role in maintaining plasma osmotic pressure, neutralizing toxins, and transporting therapeutic agents¹³. Therefore, albumin has been investigated for its postoperative effects in several surgical fields.

In a study by Kim et al¹⁴, preoperative hypoalbuminemia was shown as a predictor of the development of AKI after brain tumor surgery. Again, in a study including 4,538 patients who underwent non-cardiac surgery, low albumin values in the preoperative period were shown as an independent predictor of the development of AKI¹⁵. Low albumin was shown as an important marker

in demonstrating the development of AKI after off-pump CABG operation by Lee et al¹⁶. In yet another study performed on 505 children who underwent congenital heart surgeries, preoperative low albumin was shown as an important predictor of postoperative AKI, in addition to factors such as prolonged CPB time¹⁷. In this study which we conducted on patients over 65 years of age who underwent cardiac surgery, we found a significant relationship between low preoperative albumin and AKI.

Lymphocytes are important cells of the immune complement system, and it has been shown that low lymphocyte levels are associated with increased stress in the body and poor general health¹⁸. In addition, the poor prognostic role of lymphopenia in atherosclerotic cardiovascular diseases is well-known¹⁹. Studies^{20,21} have found that preoperative low lymphocyte levels are significantly associated with the development of postoperative AKI in patients who underwent isolated CABG operation accompanied by CPB. In our study, preoperative lymphocyte values were lower in our patient group who developed AKI, although it was not statistically significant.

Apart from albumin and lymphocyte values, CONUT score and GNRI values are calculated by formulating values such as weight and serum cholesterol parameters. Various studies have demonstrated the importance of these values in

the cardiovascular field as well as other fields of medicine. In a study by Yildırım et al²², the relationship between CONUT scores and in-hospital mortality in patients with pulmonary embolism was investigated. As a result of the multivariate analysis performed by these authors, which included 308 patients, a CONUT score >4 (OR 1.39, 95% CI: 1.146-3.424, $p = 0.015$) was shown as an independent predictor of in-hospital mortality. In a study by Wang et al²³, it was shown that the preoperative CONUT score is more predictive of prognosis in hilar cholangiocarcinoma patients than other known markers, such as neutrophil-lymphocyte ratio and prognostic nutritional index. In another study, the preoperative CONUT score was shown as an independent predictor of pulmonary complications and 1-year mortality after non-small cell lung cancer surgery²⁴. In addition, in a study⁷ including 149 patients who underwent isolated CABG surgery, severe malnutrition according to the CONUT score was found to be associated with postoperative renal complications, bleeding, and mortality.

The GNRI is a value obtained by adapting the nutritional risk index to the elderly population. In one study, the GNRI value was found to be associated with mortality and morbidity in hospitalized geriatric patients⁶. In a study by Seoudy et al²⁵, the prognostic significance of GNRI was investigated in patients who underwent transcatheter aortic valve replacement. At the end of this study, which included 953 patients, low GNRI values were found to be associated with all-cause mortality. In a study²⁶ including 287 patients who underwent elective cardiac surgery, a GNRI below 91 was found to be associated with prolonged hospitalizations. In a study by Arai et al²⁷, including 146 patients who underwent cardiovascular surgery, a low GNRI value was found to be associated with prolonged hospitalization and later mobilization²⁷.

Two studies^{28,29} have been conducted in the field of cardiac surgery with the CONUT score and GNRI. In a recently published study by Tóth et al²⁸, the prognostic role of preoperative nutritional and hormonal parameters after cardiac surgery was investigated. In this investigation, in which 252 patients who underwent various cardiac surgeries (CABG, CABG with valve, isolated valve, combined valve, valve with aorta) were included, the mean age of the patients was determined as 64.2-11. In the analyses performed, GNRI < 91 (adjusted hazard ratio [AHR]: 4.384; 95% CI: 1.866-10.303, $p = 0.001$) and the higher CONUT

(AHR: 1.736; 95% CI: 1.736-2.866, $p = 0.031$) were identified as independent predictors of mortality²⁸. In a retrospective cohort study by Cho et al²⁹, the effect of nutritional status on one-year mortality was investigated in 1927 patients who underwent valvular cardiac surgery. Although the CONUT score has higher predictive power, GNRI has also been shown to be an important predictor of postoperative one-year mortality. Our study consisted of patients over 65 years of age who had undergone various cardiac surgeries. At the end of our study, we showed GNRI and CONUT scores as independent predictors of postoperative AKI development in addition to known risk factors for AKI.

Limitations

The most important limitations of our study were the small number of patients and that it was a retrospective study. Since it was a study on a retrospective patient group, biomarkers such as cystatin C, neutrophil gelatinase-associated lipocalin, kidney injury molecule 1, cytokines, and chemokines could not be evaluated.

Conclusions

In conclusion, AKI developing after cardiac surgery is a significant condition, and risk factors should be understood. In this study, we showed the CONUT score and GNRI values calculated in the preoperative period in patients over 65 years of age as independent predictors of the development of AKI, after cardiac surgery. Our work needs to be supported by new multicenter prospective studies.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

The authors declare that this manuscript is original, has not been published before, and is not currently being considered for publication.

Ethical Approval

The Internal Review Board approved the study protocol at the University of Health Sciences Ahi Evren Thoracic and Vascular Surgery Training and Research Hospital, in accordance with the Helsinki Declaration.

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Informed Consent

Written informed consent was obtained from all patients before their surgeries.

Authors' Contribution

All authors contributed to substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and final approval of the version to be published.

Data Availability Statement

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

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