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The role of MPV/albumin ratio in determining disease severity in acute cholangitis in the emergency medicine

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ABSTRACT

Background: We aimed to examine the relationship of mean platelet volume (MPV) / albumin ratio (MAR) with disease and disease severity in patients with acute cholangitis.

Material and Method: Cases older than 18 years of age, who applied to the emergency department and were diagnosed with acute cholangitis after detailed evaluation were included in the study.Tokyo 2018 criteria are used to determine the severity of acute cholangitis.

Result: There was a positive correlation between MAR levels and Tokyo severity,and increased MAR levels were determined as an independent predictor for each risk group.The cut-off value of the MAR level in predicting moderate risk compared to the mild risk group was found to be >20.9% with 73.3% sensitivity and 70.6% specificity (AUC±SE=0.785±0.03; +PV= 51.3%, -PV= 86.2%; p< 0.001). The cut-off value of the MAR level in predicting severe risk compared to the moderate risk group was found to be >23.2% with 77.2% sensitivity and 59.1% specificity (AUC±SE=0.744±0.03; +PV= 64.5%, -PV= 72.9%; p<0.001). Mean MAR levels were found to be higher in patients admitted to the ICU compared to those who were not admitted (25.2±6.0 vs 21.3±4.6; p<0.001) and increased MAR levels were a potential risk factor for mortality (HR= 1.09; p<0.001).

Conclusion: We found that the MAR level is a very good marker in determining the severity of acute cholangitis.

Keywords: Abdominal pain,acute cholangitis, jaundice, mean platelet volume, Tokyo 2018

INTRODUCTION

Acute cholangitis is one of the emergencies with rapid onset and high mortality (1). It is associated with obstruction and infection in the biliary system (2). The clinical situation in acute cholangitis is very variable.While the patient may present with mild symptoms and minimal findings; It can also be brought to the emergency room with widespread systemic involvement and septic shock.For this reason, the patient should be evaluated in terms of the severity of acute cholangitis at the time of admission to the emergency department.

Determining the severity in patients diagnosed with acute cholangitis allows timely and effective treatment to be made (3,4). For example, in patients presenting with severe acute cholangitis, rapid and effective biliary drainage plays a major role in improving the clinical situation and reducing morbidity and mortality (5).

Tokyo 2018 criteria are used to determine the severity of acute cholangitis. According to these criteria, it is classified into three groups as mild, moderate and severe acute cholangitis (6). When determining the severity of acute cholangitis in the Tokyo 2018 criteria, extensive systemic evaluation, extensive laboratory evaluation and radiological evaluation are required. Because of this wide evaluation, acute cholangitis severity classification may not be possible in the early period in acute cholangitis patients who apply to the emergency department. For this reason, there is a need for inexpensive and reliable markers that can be measured quickly within the first few hours of admission to the emergency department, which determine the severity of acute cholangitis.

In our literature review, we could not find any study on mean platelet volume (MPV) / albumin ratio (MAR). MPV rate is an increasing parameter in both the

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gastrointestinal system and the infection rates in other foci (7-12). Albumin is a negative acute phase reactant that decreases in case of infection.Therefore, we think that the MAR will be an index with high sensitivity and specificity in acute cholangitis.

Therefore, in this study, we aimed to examine the relationship of MAR with disease and disease severity in patients with acute cholangitis.

MATERIAL AND METHOD

Study Population

This study was planned as a retrospective study in Ankara City Hospital Internal Medicine Clinic. The study was carried out with the permission of Ankara City Hospital No:2 Clinical Researches Ethics Committee (Date: 06.07.2022, Decision No: E2-22-2155). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Cases older than 18 years of age, who applied to the emergency department with complaints such as abdominal pain, jaundice, fever, nausea, vomiting, back pain, and were diagnosed with acute cholangitis after detailed evaluation were included in the study. Patients were included in our hospital from March 2019 to January 2022 according to the order of admission, regardless of gender and age.

Cases with infection in another known focus, active rheumatic disease, acute liver failure, chronic liver failure, diagnosed malignancy, malnutrition, using immunosuppressive therapy for any reason, and severe alcohol dependence were excluded from the study. The clinical demographic findings and laboratory parameters of the patients were obtained from the electronic files of the patients.

The severity of acute cholangitis in the emergency department was determined according to the Tokyo 2018 criteria (6).

The MPV / albumin ratio was calculated by dividing the MPV level by the direct albumin level.

Statistical Analysis

Statistical analysis was performed using SPSS 20 for Windows (IBM Corp., Armonk, NY, USA). The normal distribution of data was evaluated by the Shapiro-Wilk test. Numeric variables with and without normal distribution were plotted as mean±standard deviation and median (25^{th} and 75^{th} interquartile range (IQR)), respectively. Categorical variables were indicated as numeric and percentile values. Chi-square, Yates correction and Fischer's exact tests were used for comparison of categorical data. Student-T test or Mann-Whitney U test were used for comparison of numeric variables between the two groups according to the distribution of normality. ANOVA test (post-hoc: Bonferroni test) or Kruskall Wallis H test (post-hoc: Dunn's test) were used for comparison of numeric variables between the Tokyo severity groups according to the distribution of normality. Logistic regression analysis was used to identify independent predictors of Tokyo severity and ICU admission. Cox regression analysis was used to identify independent predictors of in-hospital mortality. Diagnostic performance evaluation of MAR was done by receiver operating characteristics curve analysis and the cut-off values were determined according to the Youden index method. P values $p<0.05$ (*) were considered significant in statistical analysis.

RESULT

The study population consisted of 454 patients, 340 of which were choledocholithiasis (74.9%), 44 benign biliary stenosis (9.7%), 55 malignancy (12.1%) and 15 other causes of cholangitis (3.3%).The characteristics findings of the patients are shown in **Table 1** in detail. According to Tokyo severity, 54.6% of patients had mild acute cholangitis, 23.1% moderate, and 22.1% severe acute cholangitis. It was determined that the incidence of malignant etiology, median urea levels, median CRP levels, median procalcitonin levels, mean MPV levels and mean MAR levels were increased as Tokyo severity increased, while median platelet levels, median alanine aminotransferase (ALT) levels an mean albumin levels were decreased (**Table 1**).

In the multivariable regression model, in which the variables associated with Tokyo 2018 severity were included; independent predictors of the moderate risk group compared to the mild risk group were found to be increasing age, increasing total bilirubin, increasing procalcitonin and increasing MAR levels. Independent predictors of severe risk group compared to moderate risk group were increased urea, and increased MAR levels. According to this; compared to the mild risk group, a %1 increase in the MAR level increased the moderate risk 1.38 folds (OR=1.38; $p<0.001$), compared to the moderate risk group, it increased the severe risk 1.14 folds (OR=1.14; $p<0.001$) (**Table 2**). The cut-off value of the MAR level in predicting moderate risk compared to the mild risk group was found to be >20.9% with 73.3% sensitivity and 70.6% specificity (AUC±SE=0.785±0.03; +PV= 51.3%, -PV= 86.2%; $p< 0.001$) (**Figure A**). The cut-off value of the MAR level in predicting severe risk compared to the moderate risk group was found to be >23.2% with 77.2% sensitivity and 59.1% specificity (AUC±SE=0.744±0.03; +PV= 64.5%, -PV= 72.9%; $p<0.001$) (**Figure 1B**).

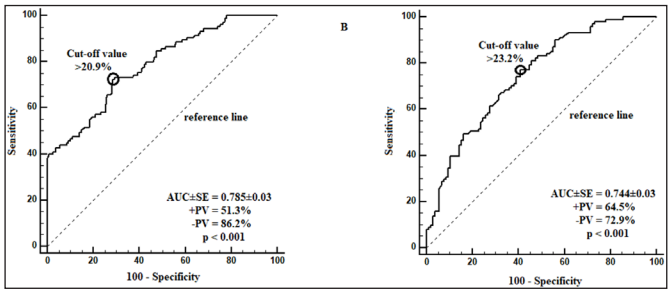

Figure 1. Diagnostic performance assessment of MAR levels in predicting moderate **(A)** and severe **(B)** of TOKYO severity

Findings related to ICU admission and mortality are shown in **Table 3** and **Table 4** in detail. MeanMAR levels were found to be higher in patients admitted to the ICU compared to those who were not admitted (25.2±6.0 vs 21.3±4.6; p<0.001) and increased MAR levels were a potential risk factor for mortality (HR= 1.09; p<0.001).

Table 1. Demographic and clinical findings of patients with acute cholangitis

Variables	All population n=454	TOKYO Severity			p
		Mild n=248	Moderate n=105	Severe n=101	
Demographicfindings					
Age, years	66.3±16.5	59.0±16.1	75.4±12.7	74.9±11.8	<0.001*
Gender, n(%)					0.500
Female	215(47.4)	114(46.0)	55(52.4)	46(45.5)	
Male	239(52.6)	134(54.0)	50(47.6)	55(54.5)	
Etiology, n(%)					0.002*
Choledocholithiasis	340(74.9)	195(78.6)	76(72.4)	69(68.3)	
Benign biliary stenosis	44(9.7)	29(11.7)	7(6.7)	8(7.9)	
Malignancy	55(12.1)	18(7.3)	15(14.3)	22(21.8)	
Other	15(3.3)	6(2.4)	7(6.7)	2(2.0)	
Duration of service, days	8(5-12)	8(5-10)	8(6-12)	8(5-15)	0.449
ICU hospitalization, n(%)	104(22.9)	21(8.5)	24(22.9)	59(58.4)	<0.001*
Duration of ICU, days	6(4-10)	5(2-7)	6(3.5-10)	6(4-11)	0.104
Laboratuar findings					
WBC, $\times 10^3$ /mL	10.2(7.6-13)	9.2(7.2-11.2)	12.9(10.2-16.2)	11.1(8-15)	<0.001*
Platelet, $\times 10^3$ /mL	240(191-312)	269.5(213.5-329)	231(191-294)	161(106-235)	<0.001*
Hemoglobin, g/dL	13.2±1.9	13.6±1.8	12.9±1.7	12.4±2.2	<0.001*
URE, mg/dL	37(27-54)	29(23-38)	42(32-54)	66(47-89)	<0.001*
ALT, U/L	188.5(98-340)	237(123.5-392)	162(105-284)	132(69-230)	<0.001*
AST, U/L	171.5(87-307)	185(90-329.5)	155(95-278)	135(77-259)	0.145
ALP, U/L	253.5(184-420)	240.5(168.5-391)	310(199-457)	257(194-354)	0.021*
GGT, U/L	445(245-708)	532(267.5-769)	457(272-741)	330(181-511)	<0.001*
Total bilirubin, mg/dL	4.6(2.9-7)	3.7(2.2-5.8)	5.9(4.1-8.4)	5.6(3.9-9.6)	<0.001*
Direct bilirubin, mg/dL	3.2(1.9-5.1)	2.5(1.3-4)	4.2(2.6-5.9)	4.1(2.8-6.9)	<0.001*
Albumin, g/dL	39.4±5.3	42.1±3.9	37.7±4.8	34.5±4.8	<0.001*
CRP, mg/dL	60(24-120)	34(17-87)	90(48-132)	110(57-179)	<0.001*
Procalcitonin, mcg/L	0.7(0.2-5.5)	0.3(0.1-1.6)	1.6(0.3-7.4)	5.4(1-32.1)	<0.001*
INR	1.2±0.5	1.1±0.2	1.2±0.1	1.6±0.5	<0.001*
MPV, fL	8.5±1.1	8.2±0.8	8.7±1.2	9.2±1.3	<0.001*
MAR	22.2±5.3	19.5±2.3	23.5±4.8	27.4±6.3	<0.001*
Composite outcome, n(%)	56(12.3)	8(3.2)	13(12.4)	35(34.7)	<0.001*
Mortality, n(%)	25(5.5)	4(1.6)	4(3.8)	17(16.8)	<0.001*
Duration of hospitalization, day	9(6-13)	8(6-11)	10(6-13)	13(8-18)	<0.001*

Data are mean±standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Bold characters show the difference between groups. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CRP, C reactive protein; GGT, gamma glutamyl transferase; ICU, intensive care unit; INR, international normalized ratio; MAR, MPV to Albumin ratio

Table 2. Independent predictors forTOKYO severity

Variables	OR	95% CI		p
		Lower	Upper	
TOKYO Severity				
Moderate (ref: mild)				
Age	1.08	1.05	1.11	<0.001*
Total bilirubin, mg/dL	1.20	1.10	1.30	<0.001*
Procalcitonin, mcg/L	1.04	1.01	1.07	0.013*
MAR	1.38	1.22	1.57	<0.001*
Nagelkerke R2= 0.528, p< 0.001				
Severe (ref: moderate)				
UREA, mg/dL	1.03	1.02	1.05	<0.001*
MAR	1.14	1.07	1.22	<0.001*
Nagelkerke R2= 0.395, p< 0.001				

*p<0.05 indicates statistical significance. Abbreviations: CI, confidence interval; MAR, MPV to Albumin ratio; OR, odds ratio.

Table 5. Independent predictors for endpoints

Variables	OR	95% CI		p
		Lower	Upper	
ICU admission				
Age	1.03	1.01	1.05	0.016*
Etiology, n(%)				
Bening	ref			
Malignancy	2.78	1.39	5.54	0.004*
Tokyo Severity				
Mild	ref			
Moderate	1.96	0.97	3.98	0.062
Severe	9.48	4.96	18.14	<0.001*
MAR	1.08	1.03	1.06	0.002*
Nagelkerke R2= 0.380, p< 0.001				
Mortality	HR			
Etiology, n(%)				
Bening	ref			
Malignancy	2.62	1.03	6.64	0.043*
ICU admission	5.14	1.05	10.41	0.018*
MAR	1.05	1.01	1.10	0.021*
-2Log Likelihood=188.2, p<0.001				

*p<0.05 indicates statistical significance. Abbreviations: CI, confidence interval; MAR, MPV to Albumin ratio; HR, hazard ratio; ICU, intensive care unit; OR, odds ratio.

Table 3. Factors associated with hospitalization of the intensive care unit in patients with acute cholangitis

Variables	ICU admission		p
	No n=350	Yes n=104	
Demographic findings			
Age, years	63.8±16.7	74.8±12.6	<0.001*
Gender, n(%)			0.999
Female	166(47.4)	49(47.1)	
Male	184(52.6)	55(52.9)	
Etiology, n(%)			<0.001*
Benign	320(91.4)	79(76.0)	
Malignancy	30(8.6)	25(24.0)	
TOKYO severity, n(%)			<0.001*
Mild	227(64.9)	21(20.2)	
Moderate	81(23.1)	24(23.1)	
Severe	42(12.0)	59(56.7)	
Duration of service, days	8(6-11)	7(1-13)	0.003*
Duration of ICU, days	-	6(4-10)	-
Laboratuar findings			
WBC, x10^3 /mL	10(7.5-12.6)	11.45(8.4-14.85)	0.007*
Platelet, x10^3 /mL	247.5(197-315)	215(145-296)	0.002*
Hemoglobin, g/dL	13.3±1.9	12.9±1.9	0.107
URE, mg/dL	34(25-48)	52(36-72)	<0.001*
ALT, U/L	201(104-348)	168.5(84-296)	0.145
AST, U/L	165(82-302)	189(98.5-308.5)	0.202
ALP, U/L	244(176-402)	311.5(198.5-444)	0.033*
GGT, U/L	464.5(251-731)	391(233.5-619)	0.172
Total bilirubin, mg/dL	4.3(2.7-6.6)	5.7(3.95-9.2)	<0.001*
Direct bilirubin, mg/dL	2.9(1.6-4.7)	4.2(2.75-6.8)	<0.001*
Albumin, g/dL	40.3±5.0	36.4±5.3	<0.001*
CRP, mg/dL	55(22-105)	100(35.5-160)	<0.001*
Procalcitonin, mcg/L	0.5(0.2-4.2)	1.95(0.4-14.95)	<0.001*
INR	1.2±0.47	1.37±0.4	0.001*
MPV, fL	8.4±1.1	8.9±1.2	<0.001*
MAR	21.3±4.6	25.2±6.0	<0.001*
Composite outcome, n(%)	3(0.9)	53(51.0)	<0.001*
Mortality, n(%)	3(0.9)	22(21.2)	<0.001*
Duration of hospitalization, day	8(6-11)	13(8-19)	<0.001*

Data are mean±standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Bold characters show the difference between groups. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CRP, C reactive protein; GGT, gamma glutamyl transferase; ICU, intensive care unit; INR, international normalized ratio; MAR, MPV to Albumin ratio

Table 4. Factors associated with in-hospital mortality in patients with acute cholangitis

Variables	Survival		Univariable Regression			
	Alive n=429	Exitus n=25	HR	95% CI lower	95% CI upper	p
Demographic findings						
Age, years	65.8±16.5	74.3±14.4	1.02	0.99	1.05	0.228
Gender, n(%)						
Female	206(48.0)	9(36.0)	ref			
Male	223(52.0)	16(64.0)	1.10	0.46	2.61	0.831
Etiology, n(%)						
Bening	387(90.2)	12(48.0)	ref			
Malignancy	42(9.8)	13(52.0)	5.38	2.30	12.60	<0.001*
TOKYO severity, n(%)						
Mild	244(56.9)	4(16.0)	ref			
Moderate	101(23.5)	4(16.0)	1.54	0.38	6.27	0.547
Severe	84(19.6)	17(68.0)	4.36	1.39	13.69	0.012*
Duration of service, days	8(5-12)	9(1-15)	1.04	1.01	1.08	<0.001*
ICU hospitalization, n(%)	82(19.1)	22(88.0)	12.08	3.50	41.76	<0.001*
Duration of ICU, days	6(4-9)	4.5(2-13)	0.95	0.90	1.01	0.115
Composite outcome, n(%)	31(7.2)	25(100.0)	52.60	4.40	635.50	0.010*
Duration of hospitalization, day	9(6-13)	11(5-20)	-	-	-	-
Laboratuar findings						
WBC, x10^3 /mL	10.1(7.6-12.9)	11.8(7.9-15.3)	1.02	0.96	1.08	0.583
Platelet, x10^3 /mL	240(193-308)	219(152-355)	1.00	1.00	1.01	0.166
Hemoglobin, g/dL	13.3±1.8	11.8±2.4	0.77	0.64	0.94	0.010*
URE, mg/dL	36(26-53)	44(36-87)	1.02	1.01	1.03	0.001*
ALT, U/L	207(109-348)	71(38-108)	0.99	0.98	1.00	<0.001*
AST, U/L	175(91-311)	115(58-222)	1.00	0.99	1.00	0.147
ALP, U/L	249(179-393)	415(282-518)	1.00	1.00	1.00	0.788
GGT, U/L	457(256-710)	308(169-583)	1.00	1.00	1.00	0.314
Total bilirubin, mg/dL	4.5(2.8-6.9)	7.9(4.5-11.1)	1.02	0.97	1.08	0.366
Direct bilirubin, mg/dL	3.1(1.8-4.9)	5.8(3.2-8.4)	1.04	0.97	1.11	0.296
Albumin, g/dL	39.8±4.9	31.8±6.5	0.84	0.79	0.90	<0.001*
CRP, mg/dL	59(24-119)	96(29-131)	1.00	1.00	1.01	0.521
Procalcitonin, mcg/L	0.6(0.2-5.5)	1.3(0.6-5.3)	1.00	0.98	1.01	0.719
INR	1.2±0.4	1.5±0.4	1.05	0.61	1.82	0.864
MPV, fL	8.5±1.1	8.9±1.3	1.06	0.77	1.46	0.721
MAR	21.8±4.6	29.6±9.0	1.09	1.05	1.13	<0.001*

Data are mean±standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Bold characters show the difference between groups. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CRP, C reactive protein; GGT, gamma glutamyl transferase; ICU, intensive care unit; INR, international normalized ratio; MAR, MPV to Albumin ratio

DISCUSSION

In this study, we examined the relationship between acute cholangitis and MAR and the role of MARin determining the severity of acute cholangitis. In our opinion, this study is the first study in this field.

We did not find any study on the MAR in any field. Although MPV levels have been studied in many disease groups, we could not find any study on acute cholangitis. In the study conducted by Şeker et al. (13) in a limited number of cholecystitis cases, MPV levels were found to be lower in acute cholecystitis cases compared to chronic cholecystitis cases. Bozkurt et al. (14), in a study conducted in acute appendicitis cases, found that MPV level was not a good marker for the diagnosis of acute appendicitis. In a study in inflammatory bowel disease, MPV was found to be a good marker for the activity of inflammatory bowel disease (8). There are also studies showing the relationship between mpv and mortality in intensive care patients (15).

When we examine the studies made with the indexes created with albumin, we often come across studies on the CRP/albumin ratio. In a study conducted by Behera et al. (16) in patients with acute pancreatitis, it was determined that the CRP/albumin ratio was correlated with prognostic scores such as Ranson and Atlanta, which predict the prognosis of acute pancreatitis. In a study of 876 people including ulcerative colitis and crohn's patients, CRP/albumin ratio was found to be associated with inflammatory bowel disease disease activity (17). Apart from these studies, it has been determined that the CRP/albumin ratio is closely related to prognosis in many gastrointestinal system malignancies (18-22).

In our study, when we classified acute cholangitis patients according to Tokyo 2018, the MAR level was found to be highest in patients with severe acute cholangitis, lower in patients with moderate cholangitis compared to patients with severe cholangitis, and higher in patients with mild cholangitis. In our regression analysis, it was determined that the MAR level predicted the severity of acute cholangitis classification according to Tokyo 2018 separately in each group. When we reviewed a meta-analysis published in the literature, the role of procalcitonin in determining the severity of acute cholangitis was examined. Six studies were included in this study. We found that the sample size was lower in all studies than in our study.In all studies, procalcitonin level was found to be higher in severe acute cholangitis patients compared to mild and moderate acute cholangitis patients (23). In our study, similar to the above studies, procalcitonin level was found to be highest in severe acute cholangitis patients, then in moderate acute cholangitis patients and lowest in mild cholangitis patients. However, in our regression analysis, procalcitonin level was found to be associated with severe acute cholangitis, but not with mild or moderate acute cholangitis. MAR was found to be better than procalcitonin in this sense. In addition, MAR level was found to be a risk factor associated with mortality in our study, while proclacytonin was not found to be associated with mortality.

In our study, we classified acute cholangitis according to the Tokyo 2018 criteria. Although MAR level and Tokyo 2018 criteria could predict admission to intensive care unit, MAR level was found to be associated with mortality, Tokyo 2018 was not associated with mortality. When we look at this secondary result of our study, we can say that the MAR level is a marker that makes the classification of acute cholangitis severity well, and that it is also a good marker that predicts both mortality and admission to the intensive care unit.In addition, in our study, together with procalcitonin, platelet, ALT, CRP, MPV, albumin and urea levels also differed in mild, moderate and severe groups of acute cholangitis, similar to MAR levels. However, no parameter was found to be associated with mild, moderate and severe groups of acute cholangitis, similar to the MAR level in the regression analysis.

The main limitation of our study is its retrospective nature. However, vital signs, physical examination findings, laboratory tests and radiological images of our patients are recorded regularly from the emergency department to the final hospitalization. This minimizes this limitation. Another limitation of ours is that it is not known when the acute cholangitis started in the cases and how long after the symptom onset the cases were admitted to the hospital.However, considering the nature of the disease, this limitation is valid for all studies conducted in this field.

CONCLUSION

In conclusion, in our study, we found that the MAR was an index related to the severity of acute cholangitis. We found that the MAR increased with the increase in the severity of acute cholangitis and the cut-off values predicting the severity. In addition, determining the MAR as an index predicting admission to intensive care and mortality is among the secondary gains of our study. More prospective studies are needed for the MAR level to be an important predictor of the severity of acute cholangitis..

ETHICAL DECLERATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital No:2 Clinical Researches Ethics Committee (Date: 06.07.2022, Decision No: E2-22-2155).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All the authors declare that they have all participated in the design, statistical evaluation and writing and that they have approved the final version.

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