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Original Article

Red Cell Distribution Width (RDW) as a Prognostic Index in Acute Coronary Syndrome

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ABSTRACT

Background: Acute coronary syndrome is a leading cause of mortality in cardiovascular disease. Red blood cell distribution width (RDW), a component of the complete blood count, has been associated with various clinical outcomes. This study investigated the relationship between RDW and in-hospital prognosis in patients with ACS.

Methods: We included 628 consecutive patients admitted with ACS. The RDW level at admission and the following prognostic factors were extracted and recorded: in-hospital mortality, presence of malignant ventricular arrhythmia, reduction in left ventricular ejection fraction, number of major cardiovascular risk factors, presence of diabetes mellitus, duration of hospitalization, number of significantly diseased coronary vessels, type of coronary intervention (percutaneous coronary intervention, coronary artery bypass grafting, or medical follow-up), and troponin positivity (indicative of myocardial infarction). The relationship between RDW level and these parameters was analyzed.

Results: Patients were stratified into two groups based on baseline RDW level: an RDW of 14.0% or greater and an RDW of less than 14.0%. The mortality rate was significantly higher in the high-RDW group than in the normal-RDW group. Mean age, incidence of malignant ventricular arrhythmia, number of cardiovascular risk factors, and length of hospitalization were also significantly greater in patients with high RDW.

Conclusions: An elevated RDW at admission in patients with ACS is a noninvasive, readily available test that may aid in prognostic assessment and stratifying in-hospital mortality risk. This parameter may warrant consideration in future clinical guidelines. ***(Iranian Heart Journal 2026; 27(1): 6-16)***

KEYWORDS: acute coronary syndrome (ACS); red cell distribution width (RDW); in-hospital prognosis

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Red blood cell distribution width (RDW) is an indicator measured within a complete blood count. This noninvasive and readily available test has a long history of use in differentiating anemic states. RDW provides a quantitative measure of the variation in red blood cell size. Its elevation is expected in various diseases because of increased erythrocyte turnover. The reference range for RDW typically falls between 11.5% and 15%, although it can vary depending on the specific measurement method employed.[1]

RDW has been considered a prognostic inflammatory biomarker. It has been of interest in various disease settings, including cardiovascular diseases, coronary artery disease, autoimmune diseases, malignancies, multiple chronic conditions, and sepsis. Notably, the prognostic value of RDW is independent of the presence of anemia in many cases. Nonetheless, elevated RDW can also be observed in specific anemic conditions such as iron deficiency anemia, megaloblastic anemia, hemolytic anemia, and following blood transfusions.[1, 2]

The association of RDW with inflammatory cytokines, the sympathetic nervous system, and the renin-angiotensin system further enhances its value as a prognostic marker. Nevertheless, the precise mechanisms underlying the relationship between high RDW and mortality in chronic and cardiovascular diseases remain under investigation and are not yet fully elucidated.[1,3]

Cardiovascular diseases remain a significant global health burden, accounting for nearly 45% of all deaths in developed societies, according to the World Health Organization (WHO).[4] Coronary artery disease is the most prevalent form of CVD, responsible for approximately 20% of these fatalities.[4] Acute coronary syndrome (ACS), a clinical manifestation of CAD characterized by acute plaque rupture or erosion leading to myocardial ischemia, is a major contributor to CAD mortality. ACS is considered in the presence of new symptoms of angina or its equivalent and electrocardiographic (ECG) changes suggestive of myocardial ischemia.[5] Despite recent advancements in diagnosis and treatment, ACS continues to pose a life-threatening challenge, particularly for high-risk patients.[5] Effective risk stratification is crucial in ACS management. It allows for the timely implementation of appropriate treatment strategies and potentially lifesaving interventions, such as invasive procedures (eg, coronary artery bypass grafting [CABG] or angioplasty) when necessary, and ultimately improves prognosis and reduces the occurrence of complications and death. While traditional risk factors, such as age, sex, smoking, and comorbidities (eg, diabetes, hypertension, dyslipidemia), have been well established, they do not fully account for risk, necessitating novel and readily available risk stratification tools.[6] For this reason, hematologic parameters, such as RDW, have emerged as promising risk factors in ACS. Studies suggest that acute inflammation in ACS, characterized by increased myeloid and sympathetic activity, triggers the release of hematopoietic stem cells from the bone marrow. This, in turn, leads to an inflammatory-hematologic cascade involving neutrophils, platelets, and lymphocytes. The consequences of this cascade include thrombotic events, cytokine release, atherosclerotic plaque instability, and, ultimately, myocyte death. These mechanisms provide a potential explanation for the link between altered hematologic parameters and adverse outcomes in patients with ACS.[7]

Previous studies suggest a link between elevated RDW and reduced red blood cell flexibility, potentially leading to impaired microcirculation and decreased tissue oxygen delivery.[8] Still, research investigating RDW as a prognostic factor in ACS has yielded conflicting results. This

inconsistency might be partially explained by differences in baseline RDW values across populations. While extensive research has been conducted on European and American populations, data specific to the Iranian population are lacking.[9,10]

Given the potential for population-specific variations in RDW values, the present study aimed to investigate the potential of RDW as an in-hospital prognostic factor in patients with ACS admitted to the cardiology department of Dezful Grand Hospital, Iran.

METHODS

Study Design and Patients

This retrospective cross-sectional study investigated 696 hospitalized patients with a spectrum of acute coronary syndrome diagnoses, including unstable angina, non–ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). The study was conducted at the cardiology department of Grand Hospital in Dezful, Iran, from June 2020 through June 2022.

Inclusion criteria were based on current ACS guidelines. Patients were identified based on the presence of new-onset angina or its equivalent symptoms, along with ECG changes suggestive of myocardial ischemia. Additionally, elevated levels of high-sensitivity troponin, a specific biomarker of myocyte necrosis, were considered diagnostic for MI. Patients who did not meet the criteria for MI were classified as having unstable angina.

All patients with ACS in the study were treated with standard ACS therapy according to valid guidelines from the first hours of their hospital stay.

Inclusion Criteria

Patients admitted to Dezful Grand Hospital with a diagnosis of ACS and an age range of 18 to 84 years.

Exclusion Criteria

Exclusion criteria included incomplete medical records and the presence of any of the following conditions: anemia (hemoglobin <12.0 g/dL for female patients or <13.0 g/dL for male patients, per World Health Organization [WHO] criteria), active inflammatory disease, or severe comorbidity (eg, severe liver, pulmonary, or renal disease).

Clinical and Prognostic Parameters

After the application of the inclusion and exclusion criteria, the study included a final sample of 628 patients (Figure 1). Demographic information (age and sex) and the presence of major coronary risk factors (hypertension, diabetes, smoking, and dyslipidemia) were collected. In addition, the following prognostic factors were extracted and recorded from patient medical records: length of hospitalization, increased plasma troponin level, in-hospital mortality, reduction in left ventricular ejection fraction (LVEF) by echocardiography, presence of malignant ventricular arrhythmia on ECG, number of significantly diseased coronary vessels by angiography, and need for invasive revascularization (percutaneous coronary intervention [PCI] or CABG).

The RDW Level

The RDW level was recorded from the complete blood count of the initial venous blood sample at the time of hospitalization (before angiography); an elevated RDW was defined as 14% or greater.[11]

Metabolic Risk Factors

Given potential fluctuations in blood glucose, lipid, and blood pressure levels during ACS, the presence of metabolic risk factors (diabetes, hyperlipidemia, and hypertension) was determined by reviewing patient medical records for the period both before and after the recent MI. Established

guidelines[12, 13] were drawn upon to define the following conditions:

Hypertension was defined as systolic blood pressure of 140 mm Hg or greater and/or diastolic blood pressure of 90 mm Hg or greater, or current use of antihypertensive medication.

A smoker was defined as an individual who had consumed 100 or more cigarettes in their lifetime.

Diabetes was defined as a fasting blood glucose level greater than 126 mg/dL, current use of glucose-lowering medication, and/or a hemoglobin A1c level of 6.5% or greater.

Hyperlipidemia was defined as a low-density lipoprotein level of 130 mg/dL or greater, total cholesterol of 200 mg/dL or greater, triglycerides of 150 mg/dL or greater, a high-density lipoprotein level of 40 mg/dL or less in men or 50 mg/dL or less in women, or current use of any lipid-lowering medication.

LVEF

LVEF was determined using the Simpson method from echocardiographic reports. According to American Society of Echocardiography guidelines, an LVEF of less than 30% was considered severe left ventricular systolic dysfunction, and an LVEF greater than 50% was considered normal.[14]

Coronary Artery Disease by Angiography

Angiography was performed within 12 to 24 hours of hospitalization via radial or femoral access in the Angiography Department of Dezful Grand Hospital. Based on established guidelines and the consensus of two interventional cardiologists at the hospital's angiography center, significant stenosis (>70% occlusion of the cross-sectional area of any major coronary artery) requiring revascularization was differentiated from minimal stenosis (<50%) managed with medical follow-up.[15] Finally, the relationship between the aforementioned parameters and the RDW level was investigated using statistical methods.

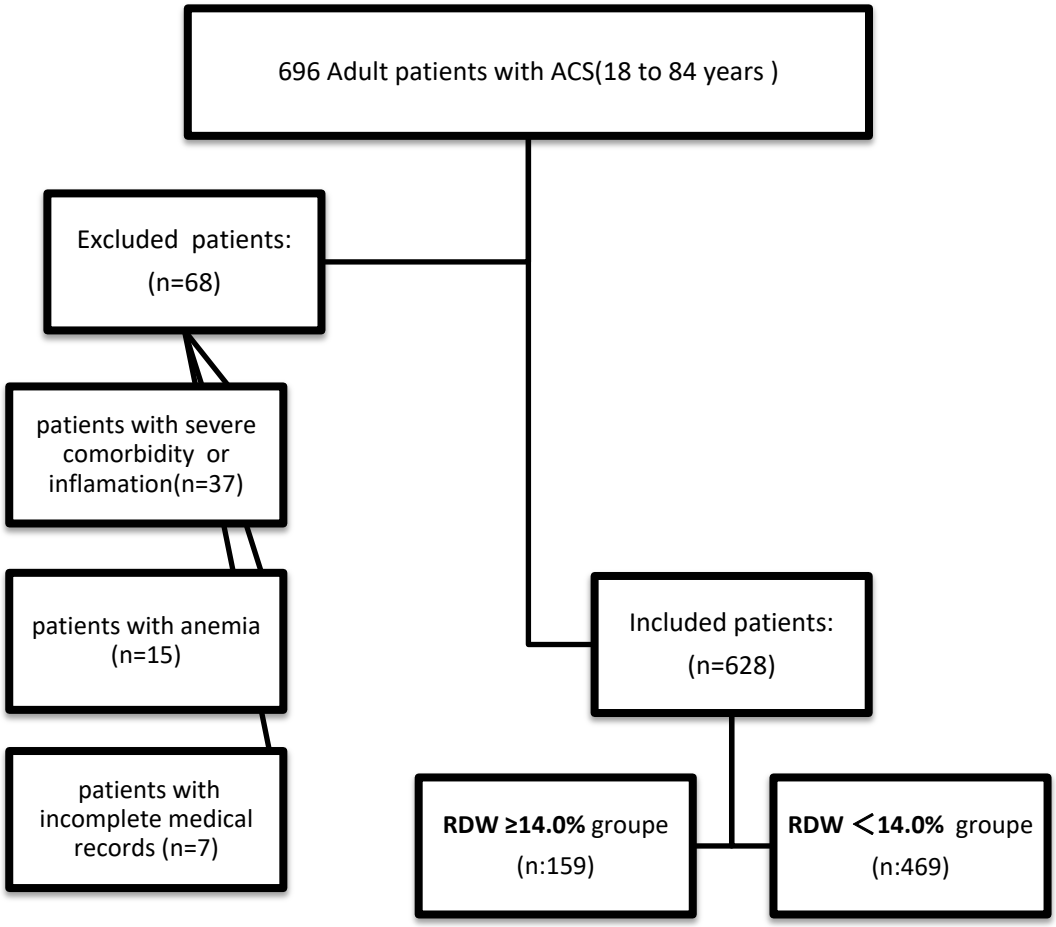

Figure 1. Flow chart of the study population
ACS: acute coronary syndrome; **RDW**: red cell distribution width

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 16.0 (IBM Corp). For continuous variables, descriptive statistics were reported as mean (SD) and median (minimum to maximum). Categorical variables were summarized using frequencies and percentages. The Shapiro-Wilk test was employed to assess the normality of continuous data distribution. Normally distributed data were compared between groups using the independent-samples *t* test. Non-normally distributed data were compared using the Mann-Whitney *U* test. The χ^2 test was used to compare categorical variables. Statistical significance was set at a *P* value of less than 0.05.

RESULTS

Tables 1 and 2 summarize the baseline characteristics, risk factors, and clinical prognostic data of the 628 patients with ACS included in the study. The mean RDW was 13.60% (SD, 1.64%). The study population had a mean age of 59.76 years (SD, 12.31 years), with 75.0% (n = 471) being male. The mean length of hospitalization was 1.66 days (SD, 1.17 days). In-hospital mortality was observed in 28 patients (4.45%).

A total of 116 patients (18.47%) had two or more cardiovascular risk factors (diabetes, hyperlipidemia, hypertension, and smoking). Diabetes was present in 286 patients (45.54%). MI, defined by positive plasma troponin levels, affected 518 patients (82.48%). Malignant arrhythmia (ventricular

tachycardia or fibrillation) occurred in 26 patients (4.14%). Additionally, 197 patients (31.37%) showed a severe decline in LVEF (≤30%).

Invasive revascularization strategies

Coronary angiography was performed in all patients. Based on coronary anatomy, PCI was performed in 516 patients (82.17%), while 89 patients (14.17%) were referred for CABG. Medical management was chosen for the remaining 23 patients (3.66%).

Table 1. Mean of RDW, age, and duration of hospitalization of 628 patients with ACS

	Mean	St. Deviation	Mode	Median	Maximum	Minimum
Age (y)	59.76	12.31	62.00	60.00	85.00	26.00
RDW (%)	13.60	1.64	12.80	13.20	25.90	7.00
Duration of hospitalization (d)	1.66	1.17	1.00	1.00	24.00	1.00

RDW: red cell distribution width; ACS: acute coronary syndrome

Table 2. Baseline characteristics and clinical prognostic data of 628 patients with ACS

		Frequency	Percent
Sex	Male / Female	471 / 157	75.00 / 25.00
Mortality	Dead	28	4.45
	Alive	600	95.55
Number of risk factors	N≥2	116	18.47
Presence of diabetes mellitus	positive	286	45.54
Ejection fraction	EF >30%	431	68.63
	EF ≤30%	197	31.37
Malignant arrhythmia	Positive	26	4.14
Intervention	PCI	516	82.17
	MFU	23	3.66
	CABG	89	14.17
Myocardial infarction	Positive	518	82.48
Number of significant diseased coronary	minimal	13	2.07
	SVD	166	26.43
	2VD	198	31.52
	3VD	251	39.98
Total		**628**	**100%**

EF: ejection fraction; PCI: percutaneous coronary intervention; MFU: medical follow-up; CABG: coronary artery bypass graft; SVD: single-vessel disease; ٢VD: double-vessel disease; 3Vd: triple-vessel disease

Patient groups and comparison

The 628 patients were stratified into two groups based on baseline RDW level: an RDW of 14.0% or greater group (n = 159) and an RDW of less than 14.0% group (n = 469). Table 3 compares the collected prognostic variables between the two groups. Figure 2 presents a comparison between the two groups for significant parameters.

Mortality and RDW

Mortality was significantly higher in the group with an RDW of 14.0% or greater than in the group with an RDW of less than 14.0% (P = 0.009). Specifically, 8.17% (13 of 159) of patients in the high-RDW group died, compared with 3.19% (15 of 469) in the normal-RDW group.

RDW and other variables

Age showed a positive correlation with RDW level (P = 0.001). The mean age was significantly higher in the high-RDW group (62.75 years) than in the normal-RDW group (58.74 y).

The occurrence of malignant arrhythmia was significantly higher in the high-RDW group (6.91%) than in the normal-RDW group (3.19%) (P = 0.041).

The multiplicity (≥2) of major risk factors (diabetes, hypertension, smoking, and dyslipidemia) was more frequently identified in patients with high RDW (23.90%) than in patients with normal RDW (16.63%) (P = 0.041).

Patients with a high RDW level had a significantly longer mean hospitalization duration (2.15 d [SD, 2.80 d]) than those with a normal RDW level (1.65 d [SD, 1.14 d]) (P = 0.029).

No significant differences were observed between the groups regarding sex, diabetes prevalence, reduced ejection fraction, type of coronary intervention (PCI/CABG or medical follow-up), troponin positivity (MI), or the number of diseased coronary arteries.

Table 3. Comparison of the prognostic variables and age by sex between the two studied groups (RDW ≥14.0% and RDW <14.0%)

		RDW ≥14.0%	RDW <14.0%	*P*
Age	Mean (y)	62.75 ± 12.73	58.74 ± 12.00	0.001
Sex	Male	118 (74.21%)	353 (75.26%)	0.791
	Female	41 (25.79%)	116 (24.74%)	
Mortality	Dead	13 (8.17%)	15 (3.19%)	0.009
	Alive	146 (91.83%)	454 (96.81%)	
Risk factors	N≥2	38 (23.90%)	78 (16.63%)	0.041
	N<2	121 (76.10%)	391 (83.37%)	
Diabetes mellitus	Diabetic patients	78 (49.05%)	208 (44.34%)	0.303
	Nondiabetic patients	81 (50.95%)	261 (55.66%)	
Ejection fraction	EF >30%	109 (68.55%)	322 (68.65%)	0.954
	EF ≤30%	50 (31.45%)	147 (31.35%)	
Malignant arrhythmia	Positive	11 (6.91%)	15 (3.19%)	0.041
	Negative	147 (93.09%)	453 (96.81%)	
Intervention (invasive or noninvasive)	PCI	122 (76.72%)	394 (84.00%)	0.070
	MFU	5 (3.14%)	18 (3.83%)	
	CABG	32 (20.14%)	57 (12.17%)	
MI (Troponin Positivity)	Positive	134 (84.27%)	384 (81.87%)	0.527
	Negative	25 (15.73%)	85 (18.13%)	
Number of Diseased coronaries	minimal	4 (2.51%)	10 (2.13%)	0.345
	SVD	37 (23.27%)	129 (27.50%)	
	2VD	44 (27.67%)	153 (32.62%)	
	3VD	74 (46.55%)	177 (37.75%)	
Duration of Hospitalization	Mean (d)	2.15 ± 2.80	1.65 ± 1.14	0.029
Total		159 (100%)	469 (100%)	

RDW: red cell distribution width; EF: ejection fraction; PCI: percutaneous coronary intervention; MFU: medical follow-up; CABG: coronary artery bypass graft; SVD: single-vessel disease; ٢VD: double-vessel disease

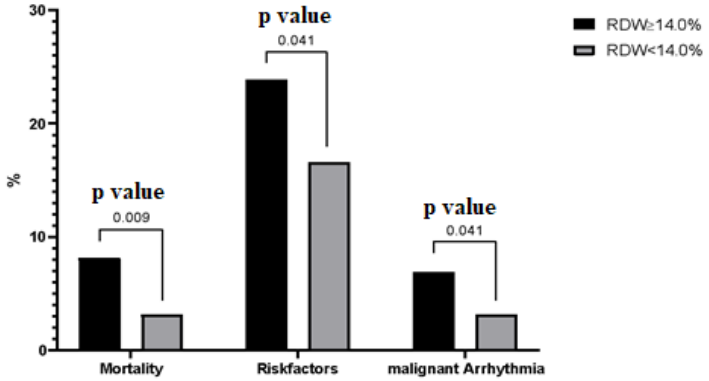

Figure 2. Prevalence of significant prognostic parameters ($P < 0.05$) between the two study groups (red blood cell distribution width ≥14.0% and <14.0%).

DISCUSSION

RDW is a parameter measured in routine hematologic assessments that reflects the variation in red blood cell size. While primarily used in the diagnosis and classification of anemias, recent research suggests its potential as a broader clinical biomarker.[15,16]

The present study examined the value of RDW as a predictor of in-hospital mortality and various prognostic indicators in patients with ACS. This study showed a significant association between elevated RDW and several prognostic factors in patients with ACS, including in-hospital mortality, advanced age, multiplicity of risk factors, malignant ventricular arrhythmia, and prolonged hospitalization. Nonetheless, we did not identify a link with other factors such as reduced LVEF, diabetes, sex, elevated plasma troponin, or the need for aggressive revascularization procedures.

The current study found a significant association ($P = 0.009$) between RDW and in-hospital mortality, which is consistent with findings from some previous studies.[16–18] The study by Pan et al[16] reported that a high RDW was associated with a 39% increase in cardiovascular disease mortality and a 27% increase in cancer-related mortality in their study population. In our study, patients with elevated RDW exhibited a higher incidence of malignant ventricular arrhythmia during hospitalization ($P = 0.041$), which can contribute to hemodynamic instability and mortality. Supporting this finding, Babes et al[19] also demonstrated a higher incidence of ventricular arrhythmia in patients with ACS with high RDW. Based on these findings, the present study suggests that continuous cardiac monitoring during hospitalization could be beneficial for patients with ACS who have elevated initial RDW levels.

Some studies suggest a link between RDW levels, reduced LVEF, and the development of heart failure in patients with ACS. In the absence of timely and effective treatment, this inflammatory cascade can lead to myocyte necrosis, ventricular remodeling, and, ultimately, heart failure. Furthermore, studies have demonstrated a correlation between RDW and inflammatory markers such as C-reactive protein and interleukin-6.[20] Our study did not identify a significant association between LVEF and high RDW between the two groups. Furthermore, elevated RDW levels were not useful in differentiating between MI and unstable angina in our patient population.

Prior studies have reported a correlation between RDW levels and both the severity of stenosis and the number of diseased

coronary vessels in patients with ACS.[21] Nevertheless, our study did not observe this association. Possible explanations for this discrepancy include confounding factors known to influence RDW levels, such as ineffective erythropoiesis, nutritional deficiencies, iron mobilization, and oxidative stress.[20, 22] These factors were not evaluated in our investigation and may have contributed to the differing results.

Despite numerous studies confirming the prognostic value of RDW in patients with ACS, the underlying mechanism for this association remains unclear.[23] Some research suggests that increased oxidative stress may play a role in atherosclerotic plaque rupture.[11, 24] An increase in RDW is expected with advancing age, higher body mass index, and the presence of metabolic disorders.[25, 26] These factors are also known risk factors for ACS and increased oxidative stress.[11, 12] Our study showed a link between advanced age and elevated RDW in patients with ACS.

The complex interplay between RDW and the underlying inflammatory processes in atherosclerosis and its associated risk factors suggests the potential utility of RDW as a prognostic marker for mortality and risk stratification in patients with ACS. Still, discrepancies exist between studies. Potential contributing factors include variations in hematologic testing methods, sample size, patient nutritional status (particularly iron, folate, and vitamin B_{12} intake), genetic predisposition, prior coronary disease history (including potential prior use of statins, anticoagulants, and antiplatelet medications), and differences in the investigated factors themselves.[26, 27]

In the current study, patients with previous coronary disease and the use of the aforementioned medications were not excluded, and the nutritional and vitamin status of patients during hospitalization was not investigated. However, in this cohort of patients with ACS, we measured RDW from the first laboratory test at admission, which may have reduced the confounding effect of anti-ischemic medications to some extent. These parameters can confound study results and necessitate a multicenter study with a larger sample size and cohort design.

Furthermore, inflammatory activity within atherosclerotic plaques can persist for months following ACS, highlighting the need for serial hematologic testing to accurately assess long-term prognosis.[26, 27] Future research directions include the development of practical treatment guidelines based on RDW levels and further investigation into the mechanisms underlying RDW elevation in patients with ACS.

CONCLUSIONS

The complex interplay between inflammation and hematologic factors in atherosclerosis has attracted significant research interest in identifying prognostic markers, including RDW. This study demonstrates the potential of RDW, a simple, noninvasive, and readily available component of the complete blood count, for predicting key prognostic factors and in-hospital mortality in patients with acute coronary syndrome. We recommend routine monitoring of RDW in patients with ACS to facilitate risk stratification and inform evidence-based treatment guidelines.

Declarations:
Funding:
This study did not receive any funding.

Conflict of Interest:
There are no conflicts of interest in relation to this research.

Authors' Contributions:
H.S. and S.R. carried out the methods. H.S., S.R., M.Kh., and Z.E. analyzed the results. H.S., S.R., M.Kh., and Z.E. contributed to the draft of the manuscript. H.S., S.R., M.Kh., and Z.E. approved the final manuscript.

Data Availability Statement:
The data that support the findings of the present study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate:
This investigation was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Ethics Committee of Dezful University of Medical Sciences (IR.DUMS.REC.1401.089). This was a retrospective medical record review; therefore, individual patient consent was waived due to the anonymous nature of the data.

Clinical Trial Number:
Not applicable.

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