

# The epidemiological and prognostic significance of the R/S Ratio in DII derivation in patients with or without ST-segment elevation

## ST segment yükselmesi olan veya olmayan hastalarda D II derivasyonunda R / S oranının epidemiyolojik ve prognostik önemi

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### SUMMARY

**Objective:** The aim of this study was to evaluate the significance of R/S ratio (RSR) in the Lead II derivation of electrocardiography (ECG) in acute coronary syndrome (ACS) patients, in regards to the complications associated with myocardial infarction (MI), three-vessel coronary artery disease (TVCAD), and mortality.

**Method:** This cross-sectional retrospective cohort study included a total of 1102 patients with ACS, who presented to our hospital's emergency department (ED) with chest pain and were admitted to the cardiology inpatient service between January 2014 and December 2017. The patients with an RSR value less than 1 were assigned to group I and the patients with RSR values greater than 1 were assigned to group II. These groups were compared in terms of age and gender; the presence of blocked major coronary arteries (BMCA), complications associated with MI, and TVCAD; Gensini Scores (GS), the levels of cardiac troponin I (cTnI), and mortality rates.

**Results:** ST-segment elevation myocardial infarction (STEMI), unstable angina (UA), and non-ST segment elevation myocardial infarction (NSTEMI) were more frequent in group I in both genders. Ischemic heart failure (IHF), ventricular tachycardia (VT), acute pulmonary edema (APE), cardiac effusion (CE), and tamponade (CT) predominated in group I. However, atrioventricular (AV) block, TVCAD, and mortality was more frequent in group II. In men, STEMI, UA, NSTEMI, branch block (BB), complications, TVCAD, BMCA, and mortality were found to be high. Atrial fibrillation (AF) occurred more commonly in NSTEMI and BBB were more common in acute inferior MI (AIMI). IHF, VT, and APE were commonly seen in acute anterior MI (AAMI). AV block was more frequent in AIMI. TVCAD was more common and the mortality rate was higher in AAMI. The BMCA was identified to be the right coronary artery (RCA) in AIMI. The most commonly blocked vessels were the circumflex artery (Cx=L1) and the left anterior descending artery (LAD=L2) in AAMI. The most commonly blocked vessel was L2 in both UA and NSTEMI.

**Conclusions:** The RSR value may become an adjunctive predictor for estimating the complications associated with MI, TVCAD, and mortality in ACS.

**Keywords:** Acute coronary syndrome, emergency department, mortality, RSR

### ÖZET

**Amaç:** Akut koroner sendrom(ACS)'lu hastaların elektrokardiografisinde(ECG) DII derivasyonunda R'in S'e oranının(RSR), myokard infarktüsü(MI) sonrası oluşan komplikasyonlar, üç damar koroner arter hastalığı(TVCAD) ve mortalite açısından etkilerinin değerlendirilmesi amaçlanmıştır.

**Yöntem:** Bu retrospektif kesitsel kohort çalışmasına, Ocak 2014-Aralık 2017 tarihleri arasında hastanemiz acil servisine(ED) göğüs ağrısı nedeniyle başvuran ve kardiyoloji kliniğine yatırılan ACS'lu 1102 hastanın verileri dahil edildi. Hastalar RSR değerinin 1'den küçük olmasına grup 1, RSR değerinin 1'den büyük olmasına grup 2 denildi. Bu gruplar yaş, cinsiyet, tıkalı majör koroner damar(BMCA), Gensini Skoru (GS), MI sonrası oluşan komplikasyonlar, kardiyak troponin I (cTnI), TVCAD ve mortalite oranları açısından karşılaştırıldı.

**Bulgular:** Her iki cinste de ST elevasyonlu MI(STEMI), unstabil angına(UA) ve non-ST elevasyonlu MI(NSTEMI) grup 1'de daha sıklıkla. Ayrıca iskemik kalp yetmezliği(IHF), ventriküler taşikardi(VT), akut akciğer ödemi(APE), kardiyak effüzyon(CE) ve tamponat(CT) yine grup 1'de ön plandaydı. Oysa atriyoventriküler(AV) blok, TVCAD ve mortalite grup 2'de daha sıklıkla. Erkeklerde STEMI, UA, NSTEMI, dal bloğu(BB), komplikasyonlar, TVCAD, BMCA ve mortalite fazla bulundu. Atrial fibrilasyon (AF) NSTEMI'da sıklıkla, BB akut inferior MI'da (AIMI) fazlaydı. IHF, VT, APE akut anterior MI(AAMI) sık tespit edildi. AV blok ise AIMI daha fazlaydı. TVCAD ve mortalite AAMI'da daha sıklıkla. BMCA AIMI'da sağ koroner arter(RCA) iken, AAMI'da circumflex arter(Cx=L1) ve left anterior descending(LAD=L2)'i en sık tıkanan damarlardı. UA ve NSTEMI'da en sık L2 tıkanığı tespit edildi.

**Sonuç:** ACS'da RSR düzeyleri MI sonrası gelişen komplikasyonlar, TVCAD ve mortalite açısından prediktif yardımcı bir değer olabilir.

**Anahtar sözcükler:** Acute coronary syndrome; emergency department; mortality; TVCAD, RSR

## INTRODUCTION

The early diagnosis and initiation of the treatment readily are of critical importance in acute coronary syndrome (ACS). Coronary artery disease (CAD) is the most common cause of mortality and morbidity in all countries. The advances in the treatment options and the increased span of the average life expectancy have led to an increase in the number of older patients with recurrent cardiovascular diseases<sup>1</sup>. The development of myocardial necrosis has been reported in animal studies after the blockage in the coronary arteries lasting longer than 30 minutes<sup>2</sup>. Every 30-minute delay in starting the reperfusion therapy after the onset of symptoms will increase the mortality rates. Percutaneous coronary intervention is a revascularization method for ACS patients and it has more favorable effects in decreasing the mortality rates in high-risk patients compared to low-risk patients<sup>4</sup>. AMI develops due to a blockage in the coronary blood flow in the previously stenosed arteries due to atherosclerosis<sup>5</sup>. Coronary atherosclerosis is recognized as a remarkably preventable disease, in which a delayed-onset is possible. CAD comprises a group of diseases, of which the incidences can be reduced when the risk factors are controlled.

Electrocardiography plays an important role in the diagnosis of ACS and the identification of high-risk patients. The size of the myocardial area at risk and the severity of ischemia are important in these patients. ECG can provide valuable information about the location and prognosis of the lesion to decide the type of coronary reperfusion therapy, as well as, it allows for making the diagnosis in ACS patients. In UA and NSTEMI, the number of derivations with ST-segment depression and the degree of depression are critical criteria for prognosis. In STEMI, the following parameters indicate a larger area of necrosis and poor prognosis, including the number

of the derivations with ST-segment elevation, the degree of the ST-segment elevation, a newly developing left bundle branch block (LBBB), right bundle branch block (RBBB) or left anterior hemiblock (LAHB), the number of derivations with reciprocal ST-segment depression along with ST elevations, and the number of derivations with Q wave<sup>6-8</sup>.

The connection of the body electrodes to ECG are called "derivations" and they determine the action potential of the heart. The derivation system of Einthoven consists of three bipolar electrodes (one positive and one negative pole or electrode) placed on the anterior surfaces of the right and left leg, and on the posterior surface of the left leg. These three derivations are aligned on the same plane and form the Einthoven triangle<sup>11</sup>. They are named as derivation I, derivation II, and derivation III. Since the derivation wave in the heart is spread from the right to the left and from cranial to caudal, Einthoven has placed the positive electrodes of these derivations on the left side of the body. Therefore, DI derivation is obtained by placing a positive electrode on the anterior of the left leg and a negative electrode on the anterior of the right leg. DII derivation is obtained by placing a positive electrode on the posterior of the left leg and a negative electrode on the anterior of the right forearm. Finally, DIII derivation is obtained by placing a positive electrode on the posterior of the left leg and a negative electrode is placed on the anterior of the right leg<sup>12</sup>.

Cardiac troponins (cTn) are structural proteins involved in the regulation of skeletal and cardiac muscle contraction together with tropomyosin. cTnT, cTnI, and cTnC complexes are located in thin filaments and allow for the calcium-mediated interaction of actin and myosin. cTn are sensitive and specific markers of cardiac muscle damage. These proteins were recognized as the standard

markers for the diagnosis of AMI and for the diagnosis and monitoring of UA by the European Society of Cardiology/American College of Cardiology (ESC/ACC) and ACC/ American Heart Association (AHA) respectively<sup>13-16</sup>.

Although a number of previous studies examined the relationship of ACS with LAHB and left posterior hemiblock (LPHB) individually, we could not find any studies in the literature, investigating both types of hemiblock and RSR based on the DII derivation. In our study, we aimed to evaluate the STEMI subgroups, which are AIMI and AAMI, NSTEMI and UA, with the RSR and cTnI values in regards to the complications associated with AMI, TVCAD, and mortality.

## MATERIAL AND METHODS

### I. Study design and population

A total of 1102 patients, consisting of 396 females and 706 males with the mean age of  $63.67 \pm 10.55$  (26-82) years, who presented to the Emergency Department of the Sivas Numune Hospital between January 2014 and December 2017 with chest pain and who were admitted to the Cardiology Clinic with the pre-diagnosis of ACS were retrospectively included in the study. The patients were excluded if the biochemistry tests, haemogram or a 12-lead ECG was not performed in the emergency department (ED); or if they did not have their angiographies or echocardiographic taken after the admission to the cardiology department. The patients were high-risk UA patients according to the Braunwald classification and the subgroups of STEMI, which were AIMI, AAMI, and NSTEMI groups<sup>17</sup>. The patients with an RSR value less than 1 were assigned to group I and the patients with RSR values greater than 1 group were assigned to group II. These groups were compared in terms of age, gender, the levels of cTnI, TVCAD, GS, and mortality. The levels of cTnI were tested at hour zero, hour 6, and hour 12 after the ED admission and recorded as troponin I, II, III respectively.

The patients who had chest pain and/or discomfort lasting at least 30 minutes, had findings of STEMI in the ECG and diagnosed in accordance with the 2013 ACCF/AHA guidelines, were included in the study<sup>18</sup>. UA/NSTEMI is diagnosed according to the criteria of the 2014 AHA/ACC Guideline for the Management of Patients With NSTEMI-ACS. Transthoracic Echocardiography (TTE) was performed in all patients to determine the presence of focal wall-motion abnormalities. A

Philips Epiq 7 Ultrasound Machine was used to perform TTE in this study.

All patients participating in the study provided their written informed consents. The study was approved by the Ethics Committee of the Cumhuriyet University, Faculty of Medicine.

The study was conducted in compliance with the Declaration of Helsinki for medical research involving human subjects and was approved by the institutional review board.

The demographic, clinical, and laboratory data of the study patients were retrospectively reviewed using the medical records in the hospital, starting from their admission to ED due to ACS.

The haemograms were performed using a Beckman Coulter Automated CBC Analyzer (Beckman Coulter, Inc., Fullerton, CA, USA).

Biochemistry tests in blood were analyzed with the Cobas 6000 (C6000-Core, Cobas c-501 series, Hitachi, Roche, USA). Performing the haemogram and biochemistry tests took 45-60 minutes.

### II. Cardiac Biomarker Analysis

The venous blood samples were obtained from the antecubital veins of the patients to measure the serum levels of cTnI using STAT Elecsys and Cobas e 411 Hitachi Roche analyzers. The cTnI levels of the patients were measured at the 0th, 6th and 12th hour of the ED admission.

### III. Electrocardiography

12-lead ECG was performed at the bedside with Cardiofax ECG-9132K (Nihon Kohden, Tokyo, Japan) at the time of admission to the ED.

### IV. Angiographic Analysis

Angiographic evaluations were performed by two experienced cardiologists who were blinded to the study. Discrepancies were resolved by consensus. The extent and severity of CAD were assessed by Gensini Scoring (GS) System (19).

### V. Gensini Scoring System

GS was calculated by multiplying the severity coefficient with the coefficient identified based on the functional importance of the myocardial area supplied by that segment. The severity coefficient was determined according to the degree of luminal narrowing as diameter reductions of 25%, 50%, 75% 90%, 99%, and 100% were given Gensini scores of 1, 2, 4, 8, 16, and 32, respectively). The coefficient determining the functional importance of the myocardial area

supplied by the respective segment was determined as follows: the left main coronary artery, 5; the proximal segment of the left anterior descending coronary artery, 2.5; the mid segment of the left anterior descending coronary artery, 1.5; the apical segment of the left anterior descending coronary artery, 1; the first diagonal branch, 1; the second diagonal branch, 0.5; the proximal segment of the circumflex artery, 2.5 (if a right coronary artery dominance existed, the coefficient would be 3.5); the distal segment of the circumflex artery, 1 (if dominant, 2); the obtuse marginal branch, 1; the posterolateral branch, 0.5; the proximal segment of the right coronary artery, 1; the mid segment of the right coronary artery, 1; the distal segment of the right coronary artery, 1; and the posterior descending artery, 1<sup>22</sup>.

### 3. Statistical Analysis

The data were analyzed with the SPSS 15 software package. Based on the sample size, the Shapiro–Wilk test was used to determine whether the variables conform to a normal distribution. The Mann-Whitney U test and Kruskal Wallis-H test were used to determine the differences between the groups as the variables did not conform to a normal distribution. When

significant differences were detected with the Kruskal Wallis-H test, a post-Hoc multiple comparison tests was performed to identify the groups with differences between. The chi-square analysis was carried out in analyzing the correlations between the groups of nominal variables. The Fisher's Exact Test was used when the expected values in the cells of the 2x2 tables were not of sufficient size, and the Spearman correlation analysis was carried out in the RxC tables using Monte Carlo Simulation. The results were interpreted at a significance level of 0.05, considering P values less than 0.05 as statistically significant.

### RESULTS

The clinical and demographic characteristics of the patients are listed in Table 1.

According to the results of the chi-square analysis of RSR; STEMI, UA, and NSTEMI were more frequent in group I in both genders. In addition, AF, BB, IHF, VT, APE, CE, and CT were also predominated in group I. However; AV block, TVCAD, and mortality were more common and statistically significant in the group II ( $p < 0.05$ , Table 2).

**Table 1:** Baseline characteristics of study patients.

Acute Coronary Syndrome					
	All patients	Patients with RSR>1	Patients with RSR<1	Z	p-value
	n:1102±SD	n:310±SD	n:792±SD		
Mean age(y)	63,67±10,55	63,26±11,02	63,83±10,36	<b>-0,507</b>	<b>0,001*</b>
Famale	396(% 35,9)	93(% 8,4)	303(% 27,5)	-	<b>0,002*</b>
Male	706(% 64,1)	217(% 19,7)	489(% 44,4)		
LVEF	51,00±13,23	48,18±12,21	52,11±13,46	<b>-4,806</b>	<b>0,001*</b>
GS	36,80±37,73	44,32±37,49	33,85±37,44	<b>-5,490</b>	<b>0,001*</b>
BMCA %	65,08±36,85	77,81±32,50	60,10±37,27	<b>-8,402</b>	<b>0,001*</b>
cTn I	1,97±4,02	2,39±3,42	1,8±4,22	<b>-5,751</b>	<b>0,001*</b>
cTn II	4,87±7,26	6,20±8,32	4,35±6,75	<b>-6,762</b>	<b>0,001*</b>
cTn III	11,52±15,72	14,92±16,90	10,18±15,04	<b>-6,668</b>	<b>0,001*</b>
TG(mg/dl)	138,83±83,79	140,98±90,55	137,98±81,03	-0,142	0,057
Chol(mg/dl)	170,90±59,74	175,70±66,79	169,02±56,67	-1,202	0,113
HDL(mg/dl)	34,11±9,46	34,72±9,76	33,87±9,34	-1,171	0,526
LDL(mg/dl)	27,86±17,29	109,43±40,96	106,79±49,59	-1,853	0,197
VLDL(mg/dl)	27,86±17,29	27,44±15,88	28,02±17,82	-0,298	0,057
BS (mg/dl)	136,00±64,44	136,73±66,31	135,71±63,74	-0,448	0,506
CK (U/L)	134,57±108,23	142,33±112,33	131,53±106,50	-2,117	0,707
CK-MB(U/L)	32,33±25,45	33,69±25,35	31,80±25,49	-1,491	0,553
Amylase U/L	78,18±37,09	82,15±39,73	76,61±35,,90	-2,042	0,666
CRP	1,88±2,81	1,79±2,85	1,91±2,79	-1,197	0,112

<b>WBC(10<sup>3</sup>/uL)</b>	10,07±3,61	9,87±3,55	10,15±3,64	-0,332	0,208
<b>MCV</b>	88,71±7,71	88,81±7,79	88,68±7,69	-0,244	0,647
<b>MCH</b>	29,33±2,30	29,29±2,46	29,34±2,24	-0,241	0,191
<b>MCHC g/dL</b>	32,86±0,75	32,87±0,70	32,86±0,77	-0,579	0,308
<b>RDW (%)</b>	15,00±2,32	15,00±2,21	15,00±2,37	<b>-8,226</b>	<b>0,001*</b>
<b>PLT</b>	246,25±74,05	237,62±77,57	249,63±72,40	-1,178	0,239
<b>MPV fL</b>	8,50±1,34	8,65±0,86	8,44±1,27	<b>-2,725</b>	<b>0,006*</b>
<b>Neu %</b>	7,21±3,56	7,42±3,84	7,13±3,44	-	<b>0,001*</b>
				<b>19,766</b>	
<b>Lymph %</b>	2,15±1,17	2,18±1,22	2,13±1,15	-0,678	0,498

ACS: Acute Coronary Syndrome, LVEF: Left Ventricular Ejection Fraction, GS: Gensini Score, BMCA: Bloded Major Coronary Artery

cTn: Cardiac Troponin, TG: Triglycerides, Chol: Cholesterol, HDL: high density lipoprotein, LDL: low density lipoprotein, VLDL: Very-low-density lipoprotein, BS: Blood Sugar, CK: Creatine Kinase, CK-MB: Creatine Kinase Muscle Brain, CRP: C-Reactive Protein, WBC: White Blood Cells, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, RDW: Red Cell Distribution Width, PLT: Platelets, MPV: Mean Platelet Volume; Neu: Neutrophil; Lymph: lymphocyte

\*p<0.05

**Table 2:** Chi-square analysis of RSR groups according to acute coronary syndrome variables

Acute Coronary Syndrome							
RSR		Patients with RSR>0,1		Patients with RSR<0,1		χ <sup>2</sup>	p-value
		n:310	%100	n:792	%100		
Gender	Famale	93	30,0	303	38,3	6,60	0,010*
	Male	217	70,0	489	61,7		
Diagnosis	UA	67	21,6	360	45,5	275,18	0,001*
	AIMI	157	50,6	55	56,9		
	AAMI	52	16,8	244	30,8		
	NSTEMI	34	11,0	133	16,8		
AF	No	239	77,1	649	81,9	10,26	0,006*
	Yes	71	22,9	143	18,1		
Branch Block	No	165	53,2	519	65,5	38,14	0,001*
	RBB	97	31,3	118	14,9		
	LBB	48	15,5	155	19,6		
Complikation	No	98	31,6	446	56,3	84,94	0,001*
	IHF	129	41,6	213	26,9		
	VT	14	4,5	56	7,1		
	AV Block	35	11,3	19	2,4		
	CE/CT	8	2,6	15	1,9		
	APE	26	8,4	43	5,4		
TVCAD	No	216	69,7	623	78,7	9,90	0,002*
	Yes	94	30,3	169	21,3		
Mortality	No	249	80,3	718	90,7	22,13	0,001*
	Yes	61	19,7	74	9,3		

UA: Unstable Angina, AIMI: Acute Inferior Myocardial Infarction, AAMI: Acute Anterior Myocardial Infarction, NSTEMI: Non ST elevation myocardial infarction, AF: Atrial Fibrillation, RBB: Right Branch Block, LBB: Left Branch Block, IHF: Ischemic Heart Failure, VT: Ventricular Tachycardia, AV: Atrioventricular, CE: Cardiac Effusion, CT: Cardiac Tamponade, APE: Acute Pulmonary Edema, TVCAD: Three-vessels Coronary Artery Disease \*p<0.05

According to the chi-square analysis of RSR, BMCA analysis was statistically significant (p<0.05, Table 3).

The chi-square analysis of RSR groups by sex showed that UA, AIMI, AAMI, and NSTEMI

were more common in men (p <0.05). The frequency of AF was not significantly different in men (p > 0.05), BB, complications, TVCAD, BMCA and mortality (p <0.05, Table 4).

**Table 3:** Analysis of acute coronary syndrome in RSR groups according to gender diagnosis and complications

Acute Coronary Syndrome						
Gender	Female		Male		$\chi^2$	p-value
	n:396	%100	n:706	%100		
Diagnosis UA Inf MI Ant MI NSTEMI	198	50,0	229	32,4	<b>40,92</b>	<b>0,001*</b>
	58	14,6	154	21,8		
	76	19,2	220	31,2		
	64	16,2	103	14,6		
AF No Yes	325	82,1	563	79,7	0,99	0,607
	71	17,9	143	20,3		
Branch Block No RBB LBB	261	65,9	423	59,9	<b>10,31</b>	<b>0,006*</b>
	57	14,4	158	22,4		
	78	19,7	125	17,7		
Komplikation No IHF VT AV Block CE/CT APE	232	58,6	312	44,2	<b>27,96</b>	<b>0,001*</b>
	110	27,8	232	32,9		
	15	3,8	55	7,8		
	12	3,0	42	5,9		
	10	2,5	13	1,8		
	17	4,3	52	7,4		
	17	4,3	52	7,4		
TVCAD No Yes	327	82,6	512	72,5	<b>14,11</b>	<b>0,001*</b>
	69	17,4	194	27,5		
Mortality No Yes	364	91,9	603	85,4	<b>10,00</b>	<b>0,002*</b>
	32	8,1	103	14,6		

\* $p < 0.05$ **Table 4:** Analysis of acute coronary syndrome diagnoses in RSR groups according to complications and variables

Acute Coronary Syndrome										
Diagnosis	UA		AIMI		AAMI		NSTEMI		$\chi^2$	p-value
	n:427	100%	n:212	100%	n:296	100%	n:167	100%		
Komplikation No IHF VT AV Block CE/CT APE	330	77,3	86	40,6	65	22,0	63	37,7	<b>372,95</b>	<b>0,001*</b>
	61	14,3	65	30,7	150	50,7	66	39,5		
	9	2,1	7	3,3	35	11,8	19	11,4		
	8	1,9	40	18,9	3	1,0	3	1,8		
	8	1,9	4	1,9	5	1,7	6	3,6		
	11	2,6	10	4,7	38	12,8	10	6		
AF No Yes	357	83,6	159	75,0	250	84,5	115	68,9	<b>50,75</b>	<b>0,001*</b>
	70	16,4	53	25,0	46	15,5	52	31,1		
Branch Block No RBB LBB	306	71,7	115	54,2	168	56,8	95	56,9	<b>35,35</b>	<b>0,001*</b>
	58	27,0	61	28,4	62	28,8	34	20,4		
	63	14,8	36	17,7	66	22,3	38	22,8		
TVCAD No Yes	423	99,1	165	77,8	133	44,9	118	70,7	<b>285,24</b>	<b>0,001*</b>
	4	0,9	47	22,2	163	55,1	49	29,3		
Mortality No Yes	413	96,7	176	83,0	238	80,4	140	83,8	<b>53,62</b>	<b>0,001*</b>
	14	3,3	36	17,0	58	19,6	27	16,2		

\* $p < 0.05$

According to the chi-square analysis of RSR groups; AF was most commonly seen in the IAMI associated with NSTEMI. While BBB is frequently seen with AIMI; IHF, VT, and APE were more frequently associated with AAMI. AV block was more common in patients with IAMI.

TVCAD and mortality rates were high in AAMI. BMCA was RCA in IAMI. In AAMI, L1 and L2 are the most frequently occluded vessels. L2 occlusion was found most frequently in UA and NSTEMI ( $p < 0.05$ , Table 5).

**Table 5:** Blocked Major Coronary Artery analysis of acute coronary syndromes

ACS										$\chi^2$	p-value
Tanı	UA		AIMI		AAMI		NSTEMI				
	n:427	100%	n:212	100%	n:296	100%	n:167	100%			
RCA	83	19,4	74	34,9	18	6,1	24	14,4	22 1, 42	0,001*	
R1	15	3,5	8	3,8	0	0	7	4,2			
R2	21	4,9	12	5,7	0	0	4	2,4			
R3	21	4,9	17	8,0	7	2,4	4	2,4			
R4	12	2,8	11	5,2	7	2,4	10	6,0			
L	48	11,2	6	2,8	15	5,1	13	7,8			
L1	48	11,2	33	15,6	53	17,9	28	16,8			
L2	87	20,4	23	10,8	133	44,9	40	24,0			
L1A	24	5,6	4	1,9	15	5,1	7	4,2			
L1B	15	3,5	8	3,8	4	1,4	4	2,4			
L1C	8	1,9	1	0,5	5	1,7	10	6,0			
L2A	28	6,6	9	4,2	22	7,4	8	4,8			
L2B	13	1,2	3	1,4	11	3,7	5	3,0			
L2C	4	0,9	3	1,4	6	2,0	3	1,8			

\* $p < 0.05$

According to BMCA chi-square analysis of RSR groups; The most frequent AF, L2 (n = 46; 4.2%) and RCA (n = 43; 3.9%); BBB was more prevalent in relation to occlusion of L2 (n = 65; 5.9%) and RCA (n = 43; 3.9%). However, the results were not statistically significant ( $p > 0.05$ ).

Statistical analysis of complications showed that IHF, VT, CE and CT were more common in L2, AV block was more common in RCA and APE was more common in L1. TVCAD and mortality were most frequently found in L2 ( $p < 0.05$ , Table 6).

**Table 6:** Friedman's Two Way ANOVA Test for Differences Between Times in Terms of Troponin Values in RSR Groups

Friedman's Two Way ANOVA										Çoklu Karşılaştırma
			n	Mean	Min	Max	SD	$\chi^2$	p-value	
RSR	RSR<0,1	0.h cTn	792	1,81	0,00	95	4,23	1203,18	0,001*	1-2 1-3 2-3
		6. h cTn		4,35	0,00	57,20	6,73			
		12. h cTn		10,18	0,01	100	15,04			
	RSR>0,1	0. h cTn	310	2,39	0,00	40,2	3,42	621,605	0,001*	
		6. h cTn		6,20	0,01	100	8,32			
		12 h cTn		14,92	0,01	100	16,90			

\* $p < 0.05$

**Table 7** : Spearman correlation coefficients for RSR groups

	RSR	
	r value	p-
LEVF	-0,145	<0,001*
GS	0,165	<0,001*
TVCAD	0,095	<0,002*
TD%	0,253	<0,001*
cTnI	0,173	<0,001*
cTn II	0,204	<0,001*
cTn III	0,201	<0,001*
BS	-0,013	>0,655
Mortality	0,142	<0,001*

\* $p < 0.05$

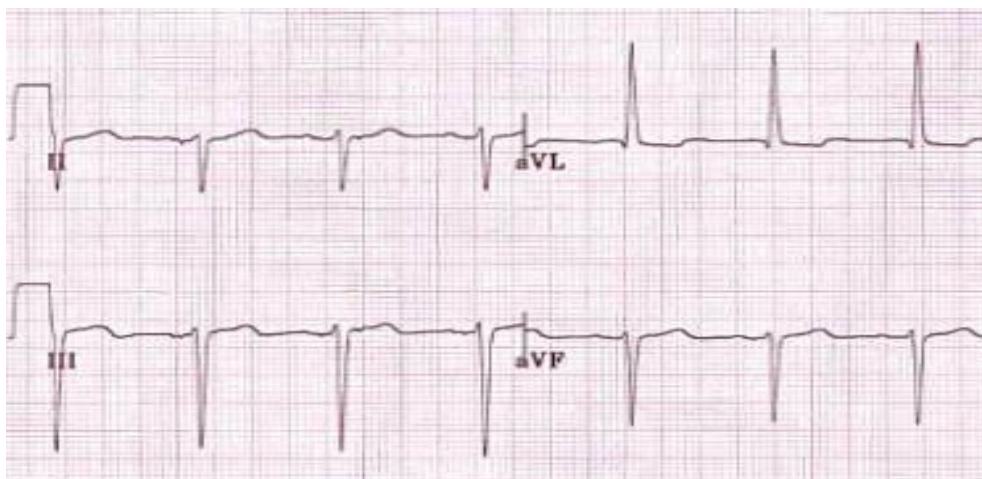
Spearman's correlation analysis showed statistically significant differences between the groups ( $p < 0.05$ , Table 7).

## DISCUSSION

There are several studies available in the literature, investigating ACS, LAHB, and LPHB either individually or together. However, we could not find any studies in the literature about RSR based on the lead II derivation. Only a few studies examined the findings in II lead of ECG at the time of ED admissions in relation with the STEMI subgroups, NSTEMI, UA, complications associated with ACS, TVCAD, and mortality. Therefore, we conducted our study in order to determine these correlations.

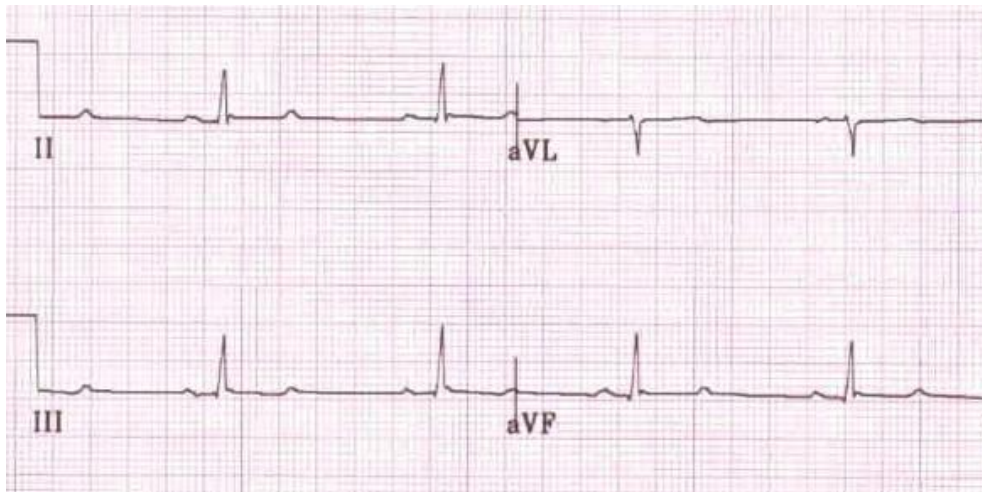
In LAHB, the posteroinferior region of the left ventricle endocardium is abnormally activated

before the anterosuperior region. After the stimulus leaves the posteroinferior fascicle of the left bundle branch, it progresses to the right and to the inferior, and usually the anterior directions for a short time, producing a Q wave in the leads I and aVL, and an R wave in the leads II, III and aVF (Figure 1). In LPHB, the stimulus leaves the bundle branch at the anterosuperior division, creating small Q waves in II, III, and aVF leads. The stimulus then progresses to the inferior direction and to the right in the electrically dominant left ventricle. This explains the S wave in I and aVL; and the R waves found in the leads II, III, and aVF (20, 21) (Figure 2).



**Figure 1:** Left anterior hemiblock





**Figure 2:** Left posterior hemiblock

In our study, DII derivation was used to determine the presence of LAHB and LPHB as these latter are determined in lead II, III, and aVF according to specific criteria. Therefore, the II lead includes both the hemiblocks and the R and S waves in the II leads without any blocks. II lead of ECG also shows the differences in the action potentials between the left arm and leg, which is equal to the total voltage of the I and II leads. Therefore, II is the lead showing the ECG waves most clearly. It is therefore used in diagnosing the cardiac rhythm disorders, in monitoring the cardiac rhythm, and in evaluating the ventricular hypertrophies. It shows inferior wall ischemia and possible Cx artery lesions in coronary artery diseases. Therefore, DII derivation was selected to be used in the study.

In a heart with a normal conduction system, the ventricular volume is determined based on the myocardial mass of the ventricles. For this reason, the mean electrical axis is calculated to determine whether the right or the left ventricle is dominant. In a healthy living organism, the left ventricle is three times larger than the right ventricle. As a result, a depolarization wave is observed in the ECG trace, mainly moving backward and to the left. Thus, large R waves are formed in leads DI, DII, DIII, and aVF<sup>22</sup>. In overt right-sided cardiomegaly, the right ventricular mass is greater than the left ventricular mass. As the right ventricle is more dominant, the depolarization wave moves forward and to the right in the ECG trace. As a result, deep S waves are observed in the leads DI, DII, DIII, and aVF. The mean electrical axis shifts to the right and to the cranial direction<sup>23</sup>. The mean electrical axis may also shift in the intraventricular conduction system blocks<sup>24</sup>.

Male gender is independently accepted as a risk factor in several studies. Coronary artery diseases are seen in males at a rate of 60%. Atherosclerotic heart diseases start developing 10-20 years earlier in male individuals with an incidence of 3-6 times higher than that of females (25). Of our study patients, 706 (64.1%) were males and 396 (35.9%) were females with a mean age of 63 years. These data were consistent with current studies.

In patients with ACS, cardiac markers such as cTnI, myoglobin, and CK-MB are important in confirming the diagnosis and in differentiating UA from NSTEMI. Elevated values of cTnI are important indicators in making the diagnosis of UA in high-risk cardiovascular patients with normal CK-MB levels, evaluated for a suspected ACS (26-28). cTnI and TnT are elevated in the reversible period of ischemia<sup>29</sup>. It is possible to identify ACS patients at risk with serial troponin measurements. In patients with high levels of cTn, it has been demonstrated that the risk of cardiac complications is higher, even if CK-MB levels are normal; and that troponins had a higher prognostic value compared to the patient's findings<sup>30,31</sup>. In the TIMI 18 study, patients with a higher cTn I level than the 99th percentile had a 3-fold higher risk of death or recurrent MI than those with a cTnI level of <0.1 ng / ml<sup>32</sup>.

In our study, the cTnI levels at hour 0, 6, and 12 were significantly higher in group 2 than those in group 1. We found that the prognosis and mortality increased in group 2 with higher cTnI levels. cTn I elevations were observed significantly higher with complications of AMI, TVCAD, and mortality. While this elevation was the highest in the STEMI subgroups followed by that in the NSTEMI group, the lowest elevation was found in the UA group with the lowest degree

of inflammation. These values were found in the univariate and multivariate time series analyses. The levels of cTnI were also positively correlated with the complications, TVCAD, and mortality. It is therefore extremely important to accurately and consistently detect the low troponin concentrations and small increases in their quantities in order to determine the critical threshold level for the follow-up and treatment, particularly in the diagnosis and prognosis of the ACS patients at risk. It is important to determine the decision-making limits for correct diagnosis in patients with ACS.

The incidence of observing RSR in the II leads have not been established yet. Even in LAHB and LPHB where RSR is  $<1$  or  $>1$ , the incidence is variable depending on the presence of CAD. In the studies on LAHB in the literature; Marriott et al.<sup>33</sup> reported the incidence as 15.2% in a 250-patient study, Scheinman et al.<sup>34</sup> reported it as 4% in a 480-patient case series, Col et al.<sup>35</sup> reported it as 6.2% in 225 patients. The frequency of an isolated LAHB was reported to be 9.9% in a 700-patient case series<sup>36</sup>. LAHB is rarely seen in patients without a history of MI, especially<sup>37</sup>. LAHB is common in acute MI patients. However, the published data is based on a limited number of patients followed-up for shorter periods. LAHB is a well-recognized complication of acute MI in 3-5% of patients. In patients with AIMI, LAHB was found to be associated with a large infarct extension and the left anterior descending CAD<sup>38,39</sup>. Because the left anterior fascicle is sensitive to very minor ischemic and necrotic alterations in the anterior descending artery due to its fine structure, LABH commonly occurs in AMI<sup>40-42</sup>.

Several studies on ECG report that LPHB occurs very rarely in the AMI patients compared to the other fascicular and branch blocks. The average incidence ranges from 0.2 to 0.4%. Scheinman<sup>43</sup> reported the incidence as 0.2% in one study and 0.4% in the other and Rizzon<sup>44</sup> reported a 0.3% incidence. Similar to these studies, similar results have been reported in the literature. All studies share the same limitation of not performing anatomical and histological examinations in a sufficient number of patients. The first likely cause of this was reported by Rosenbaum et al.<sup>45</sup> suggesting that the posterior of the left posterior bundle branch was the least sensitive part of all intraventricular conduction system. Because the blood supply comes from the branches of both the left and right coronary arteries, which are short and relatively large. The other possible cause is that if LPHB is incomplete, the ECG pattern will not show the characteristic features completely.

Therefore, it may be difficult or impossible to make a diagnosis unless the block is spontaneously formed. Finally, as the distribution of the left branch divisions can show variations, not everyone may have a separate posterior fascicle responsible for the Purkinje network in the inferior-posterior wall of the left ventricle<sup>46,47</sup>.

In this study, we did not determine the incidence as we did not focus our investigations only on the criteria of LAPH and LPHB. As II lead provides information about both of these two fascicles, we examined the gender, age, TVACD, and mortality based on RSR criteria. Although the number of study patients was higher in group I, the mean GS was low. Therefore the frequency of coronary artery involvement was low and its prognosis was found to be better compared to group II. In group II, the number of cases was low, the number of the involved coronary arteries was high, the mean EF was low, and the mean GS was high. the prognosis was determined to be worse compared to group I. In both groups, male gender was more frequent. In Group 1; AF, RBB, LBB, UA, AAMI, and STEMI were more frequent while AIMI was more prevalent in group 2. However, AV block, TVCAD, and mortality were more frequent in group II. We concluded that RSR of the DII lead could be used as an indicator in making a diagnosis and in predicting the prognosis in CAD, as well as in the follow-up of the patients.

The study by Corne et al.<sup>48</sup>, conducted on 390 males older than 30 years, reported an increased incidence of CAD in patients with LAHB when compared to the sex-matched controls. Similar studies reported an association between LAHB and the increased risk of cardiac death<sup>49-51</sup>. Intraventricular blocks associated with AMI have been studied extensively. These studies have shown that complete bundle branch blocks and incomplete fascicular blocks affect the prognosis of AMI unfavorably. Any conduction disorder developing during AMI is expected to increase the risk associated with the disease. In addition, it has been recognized that the occurrence of RBB or LBB increases the rate of mortality in AMI<sup>52-54</sup>. Castellanos et al.,<sup>55</sup> reported a high incidence of AV block in AMI in the presence of LPHB or RBBB. A bifascicular block was identified in some patients. In some other patients, a second or third-degree AV block was found (27%). All these observations supported a linkage function instead of localizing the block in the ventricle. Regardless of the location of the complete AV block, it is highlighted that it may emerge as the primary

complication in one patient or it may develop during a severe shock in the others.

Indicating the ACS-associated complications and myocardial injury, cTn I levels were low in the patients with UA with low inflammation levels in group I in our study. However, there were more findings in AAMI and NSTEMI, with a higher degree of inflammation, compared to UA. AIMI was high in group II. It was observed that the complications, TVCAD, and mortality were determined based on the types of MI. CT, CE, AF, and BBB were more common in males and in group I. BBB was more common in AAMI. In addition, hypertension, VT, APE, and IHF; commonly seen after the anterior wall MIs, were predominating in group I. This finding supports the fact that there is a tendency to develop hypertension, tachycardia, and VT during an anterior wall AMI. The frequency of 2nd and 3rd degree AV blocks in the presence of LPHB was similar to those reported in the literature in group II of our study. This finding is consistent with the tendency of inferior MI patients to develop hypotension, bradycardia, and complete block. BMCA was observed to be primarily RCA, LAD, and Cx arteries and the greater vessel structures including the right ventricular branch (R2) and LAD 2 in men. Diagonal artery (L1B) was observed to be commonly stenosed in women. RCA was found to be commonly stenosed in UA and AIMA. In AAMI, L1 was the most commonly stenosed artery followed by L1. In NSTEMI, L2 was stenosed most frequently. The prevalence and lesion severity of CAD is determined by evaluating GS. The patients with GS below 20 are categorized as having a mild CAD and the individuals with GS equal to or over 20 are categorized as severe CAD patients (56,57). For the same purpose, GS was used in our study. A significant difference was found between the GS and LVEF values of RSR <1 or RSR > 1 group categorized according to the RSR values in the DII lead. The number of patients was lower, GS was higher, and the mean LVEF was lower in Group 2. It was seen that the higher the number of the involved coronary arteries, the higher would be the Gensini scores. It was also observed that the increased scores were associated with significantly decreased LVEF depending on the area of involvement in the heart. EF was lower in both groups but lower in group II compared to group I.

Development of LABH in AIMI was correlated with significant stenoses in LAD and also correlated with multiple vessel CAD. Assali et al.<sup>38</sup> reported that of the 87 patients with AIMI,

LAHB developed in 17 (19%) patients. Significant stenosis of LAD was found in 82% of the patients with LAHB and in 21% of patients the patients without LAHB. A 159 patient study by Biagini et al. (39) reported the frequency of LAHB as 13%. The incidence of cardiac death was 2.5 times higher in patients with LAHB. During a mean of the 5-year follow-up period, the overall incidence of all-cause mortality was 1.5-fold higher in this patients group compared to the patients without LAHB. Isolated LAHB is an independent predictor of total and cardiac mortality in CAD patients without a history of MI. LPHB is almost always associated with severe CAD, in which both the anterior and posterior blood supply to the ventricular septum is unfavorably affected. A resulting wide ischemic injury covering the majority of the ventricular septum or covering at least two-thirds of the middle and posterior ventricular septum, as well as the distribution of the inferior left bundle branch and its radiations in the septum and the acute histopathological changes of the left conduction system, would affect not only the posterior septal fascicles but also the midseptal fascicles to some extent. A two- or three-vessel CAD leads to a severe insult in the cardiac tissue, leading to the development of an area of infarction involving the whole septum or covering a large area of it as confirmed with anatomical findings<sup>36, 58-61</sup>. LPHB, alone or in association with RBB, is an early complication because it occurs within a few hours or sometimes in several minutes after the onset of an acute attack. The LPHB is considered to be an ominous sign because of the 87% mortality rate. Death occurs within 48 hours following the onset of AMI as a result of the developing shock either alone or in association with acute left ventricular failure. Therefore, our findings prove that mortality is primarily related to an early manifestation of a serious pumping failure. This manifestation can readily be explained by postmortem findings indicating a severe two- or three-vessel CAD and a large area of myocardial infarction. The high mortality rates were consistent with those reported in similar studies<sup>36, 55, 58, 62</sup>.

In our study, TVCAD was detected in 263 (23.8%) patients out of 1102. Of these patients with TVCAD, 169 (21.3%) were in group I and 94 (30.3%) were in group II. Of them, 194 (27.5%) were men and 69 (17.4%) were women. TVCAD was found in 4 (0.4%) patients in the UA group, in 47 (4.3%) patients in AIMI, in 163 (14.8%) patients in AAMI, and in 49 (4.4%) in NSTEMI. The blocked arteries were most

commonly L2, L1, and RCA respectively in the order of decreasing frequency. In ACS patients, a value of RSR>1 in the DII lead is of prognostic significance for TVCAD. These findings suggest that a value of RSR>1 is a more favorable predictor in an extensive and severe myocardial ischemia compared to an RSR<1 seen in the other leads. Mortality occurred in 135 (12.2%) patients out of 1102 patients. Of these patients, 74 (9.3%) were in group I and 61 (19.7%) were in group II. Mortality occurred in 103 (14.6%) males and 32 (8.1%) females. Mortality was most common in AAMI (n=58; 19.6%), followed by AIMI (n=36; 17%). In regards to major vessel stenosis, mortality occurred most frequently in L2, RCA, and L1, respectively in the decreasing order of frequency. In the group of CAD patients with RSR>1, the factors responsible for poor prognosis and causing increased mortality are the presence of TVCAD, high GS, and low EF. The co-existence of these conditions increase the need for these patients to undergo coronary bypass surgery and may contribute to a worse prognosis. In a patient with a confirmed ACS with characteristic clinical manifestations, RSR>1 may be an independent predictor of TVCAD and mortality.

## 6. Study limitation

The major limitations of the study were its single-center and retrospective design, along with the difficulties in retrieving the data. We could not collect information on the medication use of the patients, any presence of a secondary living, and the risk factors of CAD. The main limitations were inability to collect the ECG and cTn data of the patients after admission to the emergency department and the inpatient hospitalization.

## CONCLUSION

In this study, we found that cTnI, GS, LVEF, TVCAD, and mortality increased based on whether the RSR values in the DII lead were lesser or greater than 1 in patients with ACS. Compared to the other groups, the increase in the level of cTnI occurred at a lesser degree in cases with a smaller area of involvement in the myocardium, such as UA. It was observed that the levels of cTnI were elevated more in STEMI compared to those in NSTEMI. These findings suggest that cTnI is correlated with the extent of myocardial involvement in CAD patients in group I with RSR>1 and that its levels are elevated in association with the inflammatory events emerging in AMI. In the group with RSR > 1 and above, the number of patients was low and they had a poor prognosis. In this group, 2nd and 3rd degree AV blocks, mortality, TVCAD, AIMI, and

GS were high. In the RSR <1 group, the number of patients were higher. The number of complications was higher in this group based on whether the diagnosis was AAMI or NSTEMI. However, the prognosis was good in these patients as GS were lower and LVEF were higher. RSR is similar to cTnI in the sense that it may be a prognostic factor for estimating the complications associated with AMI and for predicting TVCAD and mortality. We are of the opinion that RSR warrants further research in ACS patients.

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