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R-wave amplitude changes measured by electrocardiography during early transmural ischemia

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Abstract

Background: Changes in the amplitude of the R wave (RWA) on the electrocardiogram (ECG) have been described during acute myocardial ischemia and infarction. However, this has not been well studied in a controlled setting. We hypothesized that significant increase in RWA occurs during early transmural myocardial ischemia.

Methods: We prospectively evaluated changes in RWA in 50 patients during brief episodes of transmural ischemia induced by first balloon occlusion (mean, 38 seconds at 6-10 atmospheric pressures) during elective percutaneous coronary intervention. We recorded 12-lead ECGs at 20-second intervals before and during balloon inflation in 16 right coronary arteries, 14 left circumflex arteries, and 20 left anterior descending arteries. R wave amplitude was digitally measured in each of the 12 leads in every ECG using the ECG interval editor (General Electric HC, Menomonee Falls, WI). Intracoronary (IC) ECGs were also recorded in 4 patients. The mean of the RWA in each lead before balloon inflation was compared to the mean RWA during balloon inflation.

Results: R wave amplitude significantly increased during balloon inflation from baseline in limb leads I, II, aVL, and all the precordial leads with the exception of lead V_1. The RWA increase did not reach statistical significance in leads III, aVF, and V_1. Mean RWA increase was consistent in all leads except aVR during the brief episodes of ischemia during initial balloon inflation because of the inverse polarity of this lead. The increase in RWA was seen in most patients (mean, 75%) in whom transmural ischemia was induced by first balloon inflation. Besides, the RWA showed an increase from baseline in 3 patients who had IC-lead recordings.

Conclusion: R wave amplitude increases significantly in precordial leads (V_2-V_6) and limb leads (I, II, aVL) of the surface ECG during brief episodes of transmural ischemia. The increase in RWA might be consistent with the expansion of the left ventricular cavity during ischemia and/or alterations in conduction that are intrinsic to the myocardium.

Introduction

Increased R wave amplitude (RWA) on the surface 12-lead electrocardiogram (ECG) has been associated with various clinical conditions causing myocardial ischemia such as dynamic exercise in patients with coronary artery disease (CAD),[1-3] acute ischemia,[4] myocardial infarction,[5,6] coronary artery spasm,[7-9] and Prinzmetal angina.[10,11] The RWA changes that occur after exercise have also been used for the improved diagnosis of CAD.[1,12]

Changes in RWA during balloon angioplasty have been reported in several studies in the past with variable results. Some noted an increase in RWA during balloon inflation,[13] others reported a decrease,[14] whereas others reported biphasic changes.[15] In our study, we used a sensitive automated system and systematically examined the RWA changes on the surface 12-lead ECG during myocardial ischemia induced by acute balloon occlusion of epicardial coronary arteries in patients presenting for elective percutaneous coronary intervention (PCI). In addition, we postulated on the mechanism of the increment in RWA during hyperacute ischemia by using intracoronary (IC)-ECG recordings.

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Methods

Between August 2003 and April 2005, patients with stable angina, signs of ischemia on stress testing, or nonconclusive, noninvasive perfusion imaging in the setting of angina or decreased exercise tolerance were referred to a single center cardiac catheterization laboratory for coronary angiography and elective intervention when needed. Patients with epicardial atherosclerotic CAD were prospectively enrolled. After signing informed consent for the procedure as well as a separate consent form approved by the hospital institutional review board, patients were prepared and draped for elective PCI in standard fashion. Patients with acute coronary syndrome, chronic total occlusion of the coronary artery, myocardial infarction, left bundle branch block, right ventricular pacing, and angiographically evident collateral blood flow were excluded. The 12-lead ECGs were recorded using the MAC-8 Marquette (GE Medical Systems, Menomonee Falls, WI) ECG cart with radiolucent electrodes placed in standard fashion.

A baseline ECG was obtained before the procedure, and conscious sedation was also administered. Sedation consisted of midazolam and/or opioid analgesics (dilaudid, morphine, or fentanyl) and administered by the intravenous route in all patients. Angiography was performed using nonionic (Optiray 350 [ioversol], Mallinckrodt, St Louis, MO) contrast dye in all patients. The duration and pressure of balloon inflation, the number of inflations, and the choice of interventional equipment, including the balloon and stent, were left to the discretion of the interventional cardiologist performing the procedure. All balloon inflations were temporarily occlusive in the treated coronary arteries.

The ECGs were obtained during balloon inflation at 19-second intervals. This was typically the minimum time interval required to record an ECG, including the 10 seconds of data recorded on a standard 12-lead MAC-8 Marquette ECG cart. For consistency, the ECG data from the first balloon inflation was analyzed in this study. The ECGs obtained on 50 patients consecutively enrolled in the current study were digitally analyzed using the ECG interval editor (IE) version 005D.02 (General Electric HC, Menomonee Falls, WI). The IE automatically measured the RWA as the vertical distance from the PR segment (isoelectric line) to the peak of the QRS complex. The RWA was measured to the nearest 10^{-2} mm by the IE automated system. To explore mechanisms of RWA changes during transmural ischemia, IC-ECGs were also recorded from 4 patients during baseline and balloon inflation. Recordings were made from the angioplasty guidewire placed distal to the balloon occlusion, and lead V_1 was calibrated with a 1.0 mV standard. Simultaneous RWA recording in the other leads from the surface ECG was done. These recordings were again measured automatically by the IE system.

Table 1
Baseline characteristics in the 50-patient cohort

Variable	N = 50 (n [%])
Demographics	
Male Sex	33 (66)
Age (y)	62 ± 12
History	
Diabetes	14 (28)
Hypertension	29 (50)
Prior MI	23 (46)
CABG	0
Medications	
ACEI	26 (52)
Aspirin	47 (94)
β-Blockers	38 (76)
GP IIb/IIIa inhibitors	31 (62)
Clopidogrel	23 (46)
CCB	7 (14)
Amiodarone	1 (12)
Vessel	
LAD	20 (40)
RCA	16 (32)
LCX	14 (28)
Ejection fraction (mean ± SD)	53% ± 9%

MI indicates myocardial infarction; CABG, coronary artery bypass graft; ACEI, angiotensin-converting enzyme inhibitors; GP, glycoprotein; CCB, calcium-channel blockers.

Table 2
Mean RWA ± SD at baseline/during balloon inflation, magnitude/direction of change in mean RWA, and proportion (%) of patients with RWA increase from baseline

Lead	Baseline RWA ± SD (mm)	Occlusion RWA ± SD (mm)	Change in RWA (mm)	*P*	Proportion, N = 50 (%)
I	6.44 ± 3.14	7.02 ± 3.25	(+) 0.58	.002	82
II	7.72 ± 4.55	8.51 ± 4.61	(+) 0.79	.029	74
III	4.23 ± 3.52	4.73 ± 4.20	(+) 0.50	.192	66
aVF	5.64 ± 4.04	6.29 ± 4.41	(+) 0.65	.103	64
aVL	4.54 ± 3.50	5.13 ± 3.41	(+) 0.59	.03	86
aVR	0.99 ± 0.95	0.91 ± 0.98	(−) 0.88	.221	42
V_1	1.30 ± 0.94	1.43 ± 1.11	(+) 0.13	.105	84
V_2	3.57 ± 2.64	4.26 ± 3.29	(+) 0.69	.002	86
V_3	8.12 ± 5.53	9.00 ± 5.91	(+) 0.88	.003	74
V_4	12.00 ± 6.62	12.93 ± 7.06	(+) 0.93	.002	84
V_5	13.23 ± 6.23	14.05 ± 6.09	(+) 0.82	.007	78
V_6	10.13 ± 4.59	10.86 ± 5.02	(+) 0.73	.004	74

Statistical analysis

Continuous variables were expressed as mean ± SD and analyzed using paired 2-tailed Student *t*-tests. Skewed variables were expressed as median (minimum, maximum). Categorical variables were summarized as percentage. The SPSS version 13.0 (SPSS Inc, Chicago, IL) computer software was used for statistical analysis.

Results

The study population consisted of 50 patients with known single-vessel CAD and preserved left ventricular function undergoing elective percutaneous coronary transluminal angioplasty. Mean age of the study population was 61 ± 12 years. The other baseline characteristics of the study population and the angiographic findings are presented in (Table 1).

Angiographic findings

All angioplasty procedures were successful according to National Heart, Lung, and Blood Institute percutaneous

transluminal coronary angioplasty registry criteria for success. Balloon occlusions were carried out on 20 left anterior descending (LAD) arteries, 16 right coronary arteries (RCAs), and 14 left circumflex (LCX) arteries. The mean total occlusion time for the first balloon inflation in our patients was 40 ± 19 seconds. Inflation pressure was to 8 ± 2 atmospheres of pressure.

Intervals and heart rate

The heart rate increased during balloon inflation (70 ± 12 beats per minute) from baseline (66 ± 10 beats per minute), $P = .06$. The mean RWA at baseline and first balloon inflation was also recorded (Table 2).

R-wave amplitude

The mean RWA increased in all precordial leads and all limb leads on the 12-lead surface ECG during first balloon inflation with the exception of limb lead aVR where the mean RWA decreased (Table 2). The increase in mean RWA reached statistical significance in limb leads I, II, aVL, and precordial leads V_2 through V_6 (Table 2). Changes in mean RWA were variable in different leads among the 50 patients included in the study. An increase in mean RWA was seen in 42% of the patients in lead aVR and in 86% of the patients in lead V_2. When averaging all the leads, there was significant increase in RWA 75% of the time (Table 2). The increase in mean RWA was higher in precordial leads V_3 through V_6 when compared to the other precordial or limb leads. The mean RWA increased more in the inferior leads (II, III, aVF) in patients who had occlusion of the RCA over those who had balloon inflation in the LAD or LCX coronary arteries. This preferential increment was also visualized in the lateral leads (I, aVL, V_5, V_6) when the LCX coronary artery was occluded. There was no difference in the mean RWA

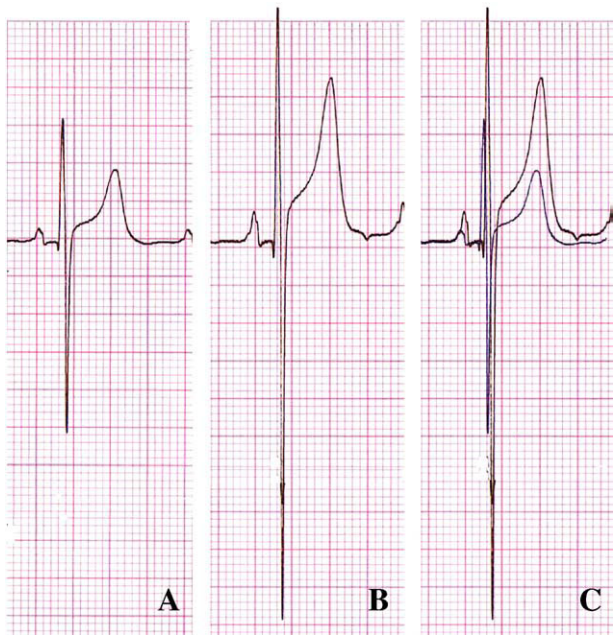

Fig. 1. Intracoronary ECG recorded at baseline (A) and 20 seconds after first balloon inflation (B). The 2 complexes seen in A and B are superimposed in C to better illustrate ischemia-induced increase in RWA. P-wave amplitude also increased reflecting left atrial dilatation because of increased LVEDD.

Table 3
Mean RWA ± SD on the surface ECG at baseline/during balloon inflation stratified according to the vessel that was intervened upon

Lead	Baseline RWA ± SD (mm)	Occlusion RWA ± SD (mm)	RWA	Vessel
I	7.12 ± 1.61	9.43 ± 2.02	+2.30	LCX
	5.84 ± 4.67	5.76 ± 4.32	−0.80	RCA
	6.22 ± 2.33	7.26 ± 2.30	+1.03	LAD
II	6.38 ± 3.53	7.19 ± 4.41	+0.82	LCX
	7.75 ± 5.15	10.80 ± 5.23	+3.05	RCA
	7.75 ± 4.13	7.28 ± 3.89	−0.46	LAD
III	2.92 ± 2.08	2.81 ± 2.32	−0.10	LCX
	4.95 ± 4.35	7.51 ± 5.35	+2.56	RCA
	4.15 ± 2.95	3.49 ± 2.60	−0.65	LAD
aVF	4.48 ± 2.93	4.74 ± 3.24	+0.27	LCX
	5.18 ± 4.52	7.86 ± 5.19	+2.68	RCA
	5.30 ± 3.61	5.42 ± 3.33	+0.12	LAD
aVL	5.73 ± 3.01	7.93 ± 3.89	+2.20	LCX
	5.18 ± 4.84	4.02 ± 4.43	−1.16	RCA
	3.70 ± 2.35	5.24 ± 2.64	+1.54	LAD
aVR	1.20 ± 0.87	1.03 ± 0.86	−0.17	LCX
	1.53 ± 1.21	1.42 ± 1.32	−0.10	RCA
	0.46 ± 0.29	0.68 ± 0.35	+0.22	LAD
V_1	1.63 ± 1.24	1.82 ± 1.27	+0.19	LCX
	1.40 ± 1.12	1.82 ± 1.55	+0.42	RCA
	0.87 ± 0.59	1.14 ± 0.48	+0.27	LAD
V_2	4.40 ± 3.04	5.61 ± 3.21	+1.21	LCX
	2.95 ± 2.59	3.55 ± 3.08	+0.60	RCA
	4.39 ± 2.69	5.31 ± 2.98	+0.92	LAD
V_3	8.09 ± 6.31	9.39 ± 6.24	+1.30	LCX
	7.35 ± 4.76	8.62 ± 4.61	+1.28	RCA
	8.85 ± 5.25	8.98 ± 5.65	+0.13	LAD
V_4	11.21 ± 5.74	13.14 ± 6.09	+1.30	LCX
	10.83 ± 6.77	13.41 ± 6.7	+2.59	RCA
	12.05 ± 6.37	13.83 ± 7.09	+1.77	LAD
V_5	10.94 ± 4.32	13.13 ± 5.00	+1.93	LCX
	13.22 ± 6.89	13.71 ± 6.78	+0.49	RCA
	13.23 ± 4.73	14.83 ± 5.10	+1.60	LAD
V_6	8.03 ± 2.55	9.57 ± 4.15	+1.53	LCX
	11.08 ± 5.58	12.20 ± 6.42	+1.13	RCA
	9.52 ± 3.47	10.54 ± 3.43	+1.01	LAD

Table 4
Mean RWA on the surface 11-lead ECG (excluding V_1) at baseline/during balloon inflation in the 4 patients who had an IC lead placed

Lead	Baseline mean RWA (mm)		Occlusion mean RWA (mm)	
I	5.82		6.22	
II	8.72		8.82	
III	5.85		4.43	
aVF	6.32		6.22	
aVL	2.83		2.91	
aVR	0.71		0.51	
IC-Lead	P1, 32.6	Mean, 71.4	P1, 102.1	Mean, 100.7
	P2, 78.7		P2, 98.4	
	P3, 25.0		P3, 55.9	
	P4, 149.6		P4, 146.5	
V_2	2.71		3.05	
V_3	6.0		6.44	
V_4	9.17		9.96	
V_5	10.11		10.79	
V_6	8.46		8.91	

The RWA (mm) in the IC-lead at baseline/occlusion in every patient as well as the mean RWA is shown.

increment in the anterior or septal leads (V^2-V^4) when LAD coronary artery was occluded (Table 3).

Intracoronary ECGs

The RWA was measured in 4 patients (1 LCX, 1 RCA, and 2 LAD) at baseline and during balloon inflation (Fig. 1). The RWA increased during balloon inflation in 3 patients compared to baseline (Table 4). The mean RWA was calculated in the IC lead as well as in the surface ECG leads. The mean RWA showed an increase in the IC-lead during balloon occlusion, 29 ± 15 mm. The increase in mean RWA in these 4 patients was seen in limb leads I (0.40 mm), II (0.10 mm), aVL (0.08 mm), and precordial leads V_2 through V_6. The increment in mean RWA in the precordial leads ranged from 0.34 to 0.79 mm.

Discussion

In the current study, we have demonstrated that RWA consistently increases during controlled transmural ischemia induced by epicardial coronary balloon occlusion in the 12-lead surface and single-lead IC-ECGs.

Several mechanisms have been proposed in previous studies to explain the alterations in RWA during ischemia. Brody's hypothesis declares that during myocardial ischemia, the left ventricle ceases to contract causing blood to pool inside the left ventricular chamber. This pooled blood will cause an increase in the voltage of the QRS complex because of either its increased conductivity or expansion of its volume.[16] This hypothesis, however, has not been conclusively established.

Feldman et al[17] considered Brody's hypothesis that in normal resting subjects, the left ventricular cavity size dictates the size of the RWA. This is supported in that during Valsalva maneuver (decreased left ventricular end-diastolic dimension [LVEDD]), the RWA decreases. On the other hand, intravenous methoxamine infusion, an α-receptor stimulant, caused an increase in LVEDD and hence an increase in the RWA on the surface ECG. Feldman[17] concluded that RWA changes are entirely a function of the proximity of the left ventricle to the electrodes on the anterior chest wall.

The ischemia experiments of David et al[18,19] showed discordant results between the RWA and left ventricular cavity size. In his experiments, coronary artery ligation in canine dogs caused a monophasic increase in echocardiographically determined LVEDD with the first beats after coronary artery ligation. This monophasic increase in cavity size, however, translated into a biphasic response in the RWA with an initial (first 30 seconds) decrease followed by an increase. David et al[18] took this experiment one step further as he induced reduction in left ventricular cavity size by obstructing vena caval inflow 3 minutes after coronary ligation. Despite this reduction in LVEDD, RWA increased even more denying a Brody-type explanation.

The biphasic response of the RWA during hyperacute ischemia correlated with a synchronous biphasic pattern in intramyocardial conduction time.[19] These biphasic effects of ischemia on both excitability and conduction are similar to the findings of progressive canine hyperkalemia.[20] In 1969, Gambetta and Childers[21] found an initial enhancement in conduction velocity because of ischemia-induced regional hyperkalemia followed by a decrease in conduction velocity within the ischemic zone. The phase of increased excitability in conduction was shown long ago to be increased by oral potassium.[15] A similar shrinkage in RWA is seen the first 2 to 4 beats after cardioversion where an efflux of potassium in coronary venous blood flow was simultaneously recorded.[22] Therefore, the initial enhancement phase of hyperkalemia is accepted as the basis for clinical supernormal excitability.[23] Childers[24] tied this acceleration in conduction to the shortening of the RWA. He thought that the enhanced conduction optimizes cancellation by opposing vectors, causing the R wave to shrink.[24] The second phase is when conduction delay develops, and RWA increases was attributed to the evasion of canceling vectors.[15,24] Childers[15,24] explains that the extended period of progressive augmentation in RWA beyond 4 minutes cannot be attributed to evasion of canceling vectors alone because evasion is intrinsically a self-limiting process. He explains this further augmentation using the solid angle theorem.[24]

$$\epsilon = (\Omega/4\pi)(TMVG^{*}C\sigma)^{25}$$

Where Ω is the solid angle at the electrode site subtending the ischemic boundary, TMVG is the transmembrane voltage gradient, and Cσ is the conductivity factor.

Acute myocardial ischemia potentially changes all the variables in the solid angle theorem equation. The alteration of variables in this equation contribute to the increment in RWA.[24]

In the present study, we used an automated digital system to calculate the RWA. This automated system is able to measure the RWA to the nearest 10^{-2} mm, a modality that is more sensitive than that used by all the previous studies where the RWA was manually and visually measured to the nearest millimeter. We showed an increase in the mean RWA in all precordial leads and limb leads with the exception of lead aVR during brief episodes of transmural ischemia induced by balloon inflation in human subjects. This decrease in mean RWA in lead aVR can be explained by the inverse polarity of this lead where, in this instance, the ECG is connected in reverse to the major direction of current flow in the heart during the cardiac cycle. Reorienting the frontal plane leads from right to left according to the Cabrera sequence[26] (III, aVF, II, −aVR, I, aVL) switches the spatial projection of lead aVR; hence, the observed decrease in mean RWA in this lead would be consistent with the increase in mean RWA in all other limb and precordial leads. Furthermore, the magnitude of the increase in the mean RWA was largest in the precordial leads closest to the chest wall, that is, V_3 through V_6 (Table 2). This finding supports Feldman's theory suggesting that the increased left ventricular diameter and proximity of left ventricular cavity to the anterior chest wall leads to the increase in RWA on the surface ECG.

The increase in RWA observed on the IC-ECGs during balloon inflation in the current study, however, suggests a different mechanism. Adopting Feldman's work, the increase in RWA should be observed on the surface and not on the IC-ECG. The RWA increase in the IC measurement suggests changes intrinsic to the myocardium or the cardiac blood pool during balloon inflation leading to conduction changes during hyperacute ischemia. The increase in RWA can be explained by the evasion of canceling vectors observed in the second phase described earlier in the work of David[19] and the solid angle theorem.[24]

The other finding that is worth mentioning is the predilection toward more increments in the magnitude of the mean RWA on the surface ECG in the leads that project the blood vessel distribution. The increase in the mean RWA was more in the inferior leads when occluding the RCA and higher in the lateral leads when the LCX was occluded. This finding supports that the mechanisms intrinsic to the myocardium determine the magnitude and direction of change in RWA rather than the proximity of the left ventricular cavity to the anterior chest wall. When the LAD artery was occluded, there was no preferential increase in the anteroseptal leads over that seen when the LCX or RCA were occluded. This latter finding can be explained by the location of the lesion that, whether it is proximal, distal, or in one of the diagonals, determines the amplitude and the direction of the change in the RWA.

Limitations

The mean RWA increase was observed in only a mean of 75% of the recorded leads in the study may be because of several factors. It is possible that some patients experienced only subendocardial ischemia instead of transmural ischemia during balloon occlusion because of collateral blood flow that was not visualized during coronary angiography, ischemic preconditioning, nitroglycerin administration, or short occlusion times. We excluded patients with chronic total occlusion and angiographically visible collaterals in the arteries being investigated. However, it is possible that some of the patients with severe coronary stenosis had collaterals not visualized by angiography. The role of collateral blood flow was entertained in the work of Holland et al.[27] He suggested that the boundary of the ischemic zone is wide in the dog where the coronary bed is rich in collaterals and narrow in the pig without collateral blood flow. This spatial influence alters the solid angle theorem reflecting on the change in the RWA. We studied only the first balloon occlusion during the percutaneous intervention to avoid the effect of ischemic preconditioning. However, this effect could not be totally eliminated because of some of the enrolled patients who may have had myocardial preconditioning because of prior exercise-induced ischemia. David et al[19] demonstrated that RWA increase reached a maximum at 116.5 seconds after coronary ligation. In our human study, because of logistical and ethical reasons, the mean duration of ischemia induced by balloon inflation was limited to 40 ± 19 seconds. Thus, we were not able to study what happens to the RWA after 1 minute of coronary artery ligation.

Conclusions and clinical implications

The RWA consistently increases during transient transmural ischemia created by balloon occlusion of epicardial coronary arteries during PCI. The voltage increased in all leads when projected in a panoramic display (III, aVF, II, −aVR, I, aVL, and V_1-V_6).[28] A predilection toward more increments in the magnitude of the mean RWA on the surface ECG in the leads that project the blood vessel distribution (RCA and LCX) was noted as well. The increase in the RWA during transmural ischemia is probably the result of mechanisms other than acute focal ischemic left ventricular dysfunction resulting in increased diameter and increased proximity of the myocardium to the chest wall.

The RWA increase should be investigated using automated systems to improve the predictive accuracy for the detection of early transmural ischemia.

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