The Giant R Wave of Acute Myocardial Infarction

Robert T. FAILLACE, M.D., Toshio AKIYAMA, M.D.,
and Winshih CHANG

SUMMARY

The common clinical electrocardiographic criteria for diagnosis of acute transmural myocardial infarction include ST segment elevation and tall, upright T waves, but do not include changes in QRS morphology. The purpose of this study was to show that development of a 50% or greater increase in R wave amplitude, the giant R wave, in patients with acute transmural myocardial infarction occurs, and also to characterize changes in QRS morphology which may aid the ECG diagnosis of acute transmural myocardial infarction. Over the past 6 years, 36 patients with an increase in R wave amplitude during acute transmural myocardial infarction were identified at the Strong Memorial Hospital Coronary Care Unit. A significant increase in R wave height (0.33 ± 0.10 to 0.97 ± 0.08 mV, $p < 0.05$), width (0.03 ± 0.00 to 0.08 ± 0.01 , $p < 0.05$) and area (0.01 ± 0.00 to 0.05 ± 0.01 mV-msec, $p < 0.05$) appeared in the same ECG lead demonstrating ST segment elevation and tall T waves during the acute phase of transmural myocardial infarction. Patients with diaphragmatic myocardial infarction showed a significant ($p < 0.05$) rightward QRS frontal plane axis shift and patients with anterior wall myocardial infarctions developed an anterior QRS axis shift in the horizontal plane during occurrence of the giant R wave.

We conclude from this preliminary study that the giant R wave may be observed during acute transmural myocardial infarction and may in part be caused by local intramyocardial conduction delay in acutely ischemic tissue as supported by an increase in the R wave width along with shifts in the frontal and horizontal plane QRS axis toward the area of acute ischemia. The giant R wave occurs in conjunction with ST segment elevation and tall T

From the Cardiology Unit, Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York, U.S.A.

Supported in part by National Heart, Lung and Blood Institute Postgraduate Training Grant HL-07220, Public Heart Service Grant HL-07496 from the National Institutes of Health, Grants-in-Aid from the American Heart Association (80-677) and the Genesee Valley Chapter of the American Heart Association.

Address for reprint: Toshio Akiyama, M.D., Cardiology Unit—Box 679, University of Rochester, NY 14642, U.S.A.

Received for publication March 9, 1984.

waves and may aid the ECG diagnosis of acute transmural myocardial infarction.

Additional Indexing Words:

Giant R wave Acute myocardial infarction
ECG diagnosis QRS morphology

ELECTROCARDIOGRAPHIC criteria used for the diagnosis of acute myocardial infarction include both ST segment elevation and tall upright T waves.^{1)–3)} Although Hellerstein⁴⁾ and Ekmekci⁵⁾ showed an increase in R wave height along with a decrease in S wave depth (“the giant R wave”) occurring during acute experimental myocardial ischemia, previous studies have not quantitatively examined changes in QRS morphology during the early phase of acute myocardial infarction in man.

The giant R wave has been reported to occur during attacks of Prinzmetal’s angina^{6),7)} together with a shift in the frontal plane axis, not representative of fascicular block, toward the area of acute ischemia.⁸⁾ Other studies have suggested that increase in R wave amplitude associated with variant angina may be a harbinger of serious ventricular arrhythmias.^{9),10)} However, only one case of the giant R wave has previously been reported to occur in a patient who developed ST elevation and hyperacute T waves during the very early phase of acute transmural myocardial infarction.¹¹⁾

The objectives of this study were to: 1) show that the giant R wave does occur in patients with acute transmural myocardial infarction and is not as rare as previously assumed and 2) to characterize changes in QRS morphology of the giant R wave.

METHODS

Patient population

Over the 6 years from 1975–81, 36 patients with an increase in R wave amplitude during acute myocardial infarction (AMI) (greater than 50% above the R wave height observed prior to acute myocardial infarction) have been identified at the Strong Memorial Hospital Coronary Care Unit by one of the authors (T.A.). Over this 6-year period, a total of approximately 740 patients with acute transmural myocardial infarction were treated at the above mentioned coronary care unit. The author (T.A.) was exposed to the electrocardiograms of about half of these 740 patients (i.e. 370 patients). From this population, 36 cases of giant R wave were found to satisfy the following criteria. The diagnosis of AMI was confirmed by development of at least

two of the following criteria: 1) symptoms suggestive of acute myocardial infarction, 2) elevation of total creatine kinase with positive MB isoenzyme and 3) development of pathologic Q waves on ECG. The electrocardiograms of the patients studied satisfied the following criteria: 1) availability of ECG prior to AMI (pre-GR), 2) availability of ECGs taken during the first 24 hours of AMI (GR), 3) availability of ECG taken at least 2 days after AMI (post-GR), except for 3 patients who died within 24 hours of the GR ECG and 4) development of increased R wave voltage (greater than 50%) during AMI. Although many initial ECG tracings seemed to have shown giant R waves, many patients were excluded from this study because their pre-GR tracings were unavailable. Patients who developed intraventricular conduction block, either complete or left or right bundle branch block or left posterior hemiblock in cases of diaphragmatic myocardial infarctions or left anterior hemiblock in cases of lateral wall myocardial infarctions (pp. 237-250, Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels, 8th Ed, Criteria Committee of the New York Heart Association, Little and Brown Co., Boston, 1973) in the pre-GR, GR or post-GR periods were excluded from the study.

ECG analysis

Of the 36 patients studied for the giant R wave, 26 had diaphragmatic, 8 had anterior and 2 had lateral wall myocardial infarctions. The morphology of the QRS-T waveform was quantitated in the lead demonstrating the largest increase in R wave amplitude. A representative ECG from the pre-GR, GR and post-GR periods was analyzed for the following parameters: QRS width, depths, widths; areas of Q, R and S waves; T wave and ST segment height; mean QRS area and the height of the R wave minus ST segment height (R-ST). The PR segment was used as the baseline for all measurements. Area was determined by assuming the shape of the Q, R, or S waves to be that of a triangle. Therefore, area (mV-msec) was computed as a product of one-half height (mV) and the width (msec). The mean QRS area was calculated as the algebraic sum of the individual Q, R and S areas. The mean QRS axis on the frontal plane was determined by using the QRS areas of leads 1 and 3. The mean QRS axis on the horizontal plane was estimated using leads V_1 and V_6 . We assumed V_6 to be located laterally on the left side at 0 degrees and V_1 anteriorly at 100 degrees on the horizontal plane. Heart rate and corrected QT interval (QT interval divided by the square root of the R-R interval in seconds) were also measured in all ECGs.

Chart review

The charts of all patients studied were retrospectively reviewed. Observations included symptoms at the time of acute myocardial infarction and

number of hours between the development of symptoms and the giant R wave tracing. Hematocrit and serum electrolytes (sodium, potassium, chloride and bicarbonate) were recorded for the pre-GR, GR and post-GR periods. Peak creatine kinase and presence or absence of CK-MB were also recorded.

Statistical analysis

Paired Student's t-test was utilized in assessing the significance of the previously described ECG measurements, serum hematocrit, and electrolytes obtained from the pre-GR, GR and post-GR periods. Statistical significance was defined as $p \leq 0.05$.

RESULTS

The giant R wave in acute inferior myocardial infarction

An example of the giant R wave occurring in the inferior leads in a patient with an acute inferior myocardial infarction is shown in Fig. 1. The electrocardiogram recorded half an hour after the onset of sustained severe substernal chest pain (Fig. 1-B) reveals a tall upright and widened R wave (the giant R wave) with little or no downward deflection in leads 2, 3 and aV_F . In addition to the giant R waves the electrocardiogram shows common electrocardiographic findings of acute inferior myocardial infarction: ST segment elevation and tall upright T wave in 2, 3 and aV_F , first degree AV block and sinus bradycardia. The frontal plane QRS axis shifts rightward from $+40^\circ$ (Fig. 1-A) to $+73^\circ$ (Fig. 1-B) in association with development of the giant R wave. The electrocardiogram recorded on the tenth

A

Fig. 1. Giant R wave in acute inferior myocardial infarction.

- A. Twelve lead electrocardiogram recorded about 1 year prior to admission shows borderline sinus bradycardia, borderline first degree AV block, mild intraventricular conduction defect and a mean frontal QRS axis of $+40^\circ$.
- B. The ECG recorded half an hour after the onset of sustained severe sub-sternal pressure reveals the giant R wave along with ST segment elevation and tall upright T wave in the inferior leads. The mean frontal QRS axis has shifted rightward to $+73^\circ$.
- C. The tracing recorded on the tenth hospital day shows new pathologic Q waves and inverted T waves in the inferior leads.

hospital day (Fig. 1-C) reveals new pathologic Q waves in 2, 3 and aV_F. These evolutionary electrocardiographic changes along with the patient's symptoms, rise of CPK to 961 international units and positive CPK-MB isoenzyme established the diagnosis of acute inferior myocardial infarction.

The giant R wave in acute anterior myocardial infarction

An example of the giant R wave occurring in the precordial leads in a patient with acute anterior myocardial infarction is shown in Fig. 2. As seen in the electrocardiogram recorded 2 months prior to acute inferior myocardial infarction (Fig. 2-A) the patient had an old inferior myocardial infarction. The electrocardiogram recorded half an hour after the onset of sustained

A

B

C

D

Fig. 2. Giant R wave in acute anterior myocardial infarction.

- A. The ECG recorded 2 months prior to acute anterior myocardial infarction reveals signs of an old inferior myocardial infarction.
- B. The ECG obtained half an hour after onset of sustained severe pressure displays a marked increase in R wave amplitude (the giant R wave), ST segment elevation and tall upright T wave in V_{2-5} .
- C. The ECG recorded 1 hour after the onset of acute myocardial infarction shows the giant R wave, ST segment elevation and tall upright T waves in V_{2-5} . Please note that S waves are no longer present in V_{2-5} .
- D. The ECG recorded on the third hospital day shows new pathologic Q waves in $V_{2,3}$ and persistent ST segment elevation in V_{1-5} .

Table I. Change in QRS-T Waveform Occurring

	QRS Width (msec)	Q			R		
		Width (msec)	Depth (mV)	Area (mV·msec)	Width (msec)	Height (mV)	Area (mV·msec)
Pre-GR n=36	.08 ±.004	.05 ±.030	-.13 ±.030**	-.006 ±.003**	.03 ±.004	.33 ±.096	.01 ±.001
GR n=36	.10 ±.006†	.03 ±.000	-.17 ±.040	-.003 ±.001	.08 ±.007†	.97 ±.084†	.05 ±.006†
Post-GR n=33	.08 ±.005*	.05 ±.010	-.54 ±.070*	-.020 ±.005*	.04 ±.010	.22 ±.049*	.007 ±.002*

All values expressed $\pm$ SEM. * $p < 0.05$ GR to Post-GR, ** $p < 0.05$ Post-GR to Pre-GR,

severe substernal pressure (Fig. 2-B) reveals tall upright T waves, a marked increase in R wave amplitude and a reduction in S wave depth in V_{2-5} . In the tracing recorded 1 hour after the onset of myocardial infarction (Fig. 2-C) the S waves, which were previously present in V_{2-5} , are no longer present and the RS complexes are now replaced by the R wave (the giant R wave). The tracing, furthermore, reveals other common electrocardiographic findings of acute myocardial infarction, such as ST segment elevation and tall upright T waves. The electrocardiogram obtained on the third hospital day (Fig. 2-D) shows new pathologic Q waves in $V_{2,3}$ and persistent ST elevation in V_{1-5} . The rise in CPK to 3,500 international units and positive CPK-MB isoenzyme on the first hospital day confirmed the diagnosis of acute myocardial infarction.

Characteristics of the giant R wave

A total of 36 patients satisfying the above criteria were identified at the Strong Memorial Hospital Coronary Care Unit over a 6-year period. The time between the onset of chest pain and the recording of the ECG registering the giant R wave was 1.9 ± 0.4 hours (mean $\pm$ SEM). Peak CPK averaged 1,420 international units.

No significant change in heart rate, corrected QT interval, mean blood pressure, or serum electrolytes was noted between the pre-GR to GR and the GR to post-GR periods. Although hematocrit was without significant change between the pre-GR and GR period, a significant fall occurred between the GR and post-GR period from $43 \pm 1\%$ to $39 \pm 1\%$, respectively ($p < 0.05$). Serum sodium decreased from 138 ± 0.7 mEq/L to 136 ± 0.7 mEq/L ($p < 0.05$) from the pre-GR to GR period, respectively.

Table I shows changes in the QRS-T wave morphology among the pre-GR, GR and post-GR ECGs in patients with diaphragmatic, anterior and lateral wall myocardial infarctions. As demonstrated, ST segment elevation

during Development of the Giant R Wave

S			Mean QRS†† (mV·msec)	ST (mV)	T (mV)	R-ST (mV)
Width (msec)	Depth (mV)	Area (mV·msec)				
.02 ±.005**	-.30 ±.087**	-.007 ±.002**	-.009 ±.005	.05 ±.022**	.13 ±.052	.257 ±.039**
.001 ±.000†	-.004 ±.006†	-.001 ±.000†	.04 ±.007†	.38 ±.042†	.46 ±.085†	.615 ±.077†
.004 ±.002	-.06 ±.038	-.001 ±.001	-.01 ±.005*	.12 ±.024*	.04 ±.054*	.106 ±.049*

† $p < 0.05$ Pre-GR to GR, †† mean QRS = mean QRS area.

and tall T waves were associated with a significant increase in the height, width and area of the R wave during the acute phase of myocardial infarction. There was also a significant increase in the difference between R wave and ST segment height (R-ST), while S wave depth, width and area were

Fig. 3. Rightward frontal mean QRS axis shift with acute inferior myocardial infarction ($n=26$).

Prior to acute inferior myocardial infarction, and therefore, prior to development of the giant R wave (Pre-GR) mean QRS axis on the frontal plane was $27 \pm 8^\circ$ (mean $\pm$ SEM). A significant rightward shift ($p < 0.05$) has occurred during the time of the giant R wave development (GR). With development of pathologic Q waves following acute inferior myocardial infarction (Post-GR), a significant leftward axis shift is observed as compared to the axis during GR ($p < 0.05$).

Fig. 4. Anterior horizontal mean QRS axis with acute anterior myocardial infarction ($n=8$).

Although it was of borderline statistical significance, an anterior shift in the horizontal QRS axis occurred from Pre-GR to GR. With the development of pathologic Q waves, a posterior shift occurred in the Post-GR ECGs as compared to GR and Pre-GR ECGs.

noted to decrease significantly in the GR ECG as compared to the control tracing. The increase in R wave width was the major contributing factor accounting for the increase in total QRS width during acute ischemia. The post-GR ECG demonstrated the development of a significant increase in Q wave depth and area. R wave depth and area, ST segment and T wave amplitude, and R-ST all significantly decreased in the post-GR ECG.

Fig. 3 demonstrates a slight, but significant rightward axis shift in the frontal plane during the GR ECG as compared to the pre-GR ECG in patients with diaphragmatic myocardial infarction. A subsequent significant leftward frontal plane axis shift occurred in the post-GR ECG. Fig. 4 shows an anterior axis shift in the horizontal plane in the GR ECG as compared to the control ECG of patients with anterior wall myocardial infarction. A posterior axis shift in the horizontal plane was observed in the post-GR ECG.

DISCUSSION

Although the giant R wave has been demonstrated to develop imme-

diately following ligation of major coronary arteries in experimental animals and has been observed to occur during attacks of Prinzmetal's angina, the clinical electrocardiographic criteria most commonly employed in the diagnosis of acute transmural myocardial infarction are ST segment elevation and tall upright T waves. Our study demonstrates a significant increase in R wave height and width occurring in the same ECG leads showing ST segment elevation and tall T waves in patients during the early phase of acute transmural myocardial infarction.

In 1950, Hellerstein and Liebow⁴⁾ recorded a marked increase in amplitude and delay of the epicardial R wave intrinsicoid deflection along with a decrease in S wave depth, ST segment elevation and hyperacute T waves 2 to 3 min following coronary artery ligation in the dog. Rakita and Prinzmetal¹²⁾ and Hamlin^{13),14)} confirmed these findings in later animal experiments. Ekmekci⁵⁾ termed this increase in R wave amplitude and width associated with acute transmural myocardial ischemia the "giant R wave". During the first 50 sec following coronary artery occlusion Holland and Brooks¹⁵⁾ observed an initial decrease in ventricular activation time and R wave amplitude indicating a transient increase in conduction velocity followed by a significant increase in ventricular activation time and R wave amplitude, indicating a marked decrease in conduction velocity. Furthermore, the ventricular activation time was found to be inversely proportional to the extracellular potassium concentration. Since potassium is known to be released from ischemic cells following coronary artery occlusion,^{16),17)} this ion was implicated as an agent at least partially responsible for altering intramyocardial conduction velocity during the course of acute ischemia. Increase in extracellular potassium is known to cause a decrease in resting membrane potential with subsequent decrease in total action potential amplitude, overshoot potential with subsequent decrease in total action potential amplitude, overshoot potential and maximum upstroke slope of the transmembrane action potential,^{18),19)} thereby causing a decrease in conduction velocity. Akiyama and Richeson²⁰⁾ demonstrated that during early transmural ischemia, the activation wavefront propagates very slowly toward the center of the ischemic zone from non-ischemic sites and that this slowly advancing wavefront persists in the ischemic tissue even after complete activation of the non-ischemic myocardium. Based upon these observations, Akiyama and Richeson postulated that temporal isolation of the ischemic zone from activation of non-ischemic myocardium results in loss of internal cancellation and that this formation of a centrally directed wavefront contributes to the genesis of the giant R wave.^{21),22)}

However, if local ischemic intramyocardial conduction delay contributes

to formation of the giant R wave, then the R wave should also be widened and the mean QRS axis (or at least the mid to terminal portion of the QRS) should be directed towards the area of acute infarction. The results of our ECG analysis conform with these predictions. Patients with diaphragmatic myocardial infarction demonstrated a significant rightward mean QRS axis frontal plane shift while patients with acute anterior myocardial infarction showed an anterior horizontal mean QRS axis shift during the ECG recording of the giant R wave. In addition, the increase in R wave height was associated with an increase in the R wave width.

An additional factor which may influence the size of the QRS amplitude is the Brody effect.²³⁾ According to Brody's theory, an increase in the conductivity of the relatively large intracavitary blood mass will tend to short circuit tangential components, but augment radial components of myocardial dipoles. Therefore, with increased left ventricular volume, the QRS amplitude will increase. Other studies have confirmed this theory.^{24), 25)} However, this is a generalized phenomenon and is not confined to leads demonstrating ST abnormalities and is not necessarily related to QRS axis shifts. The Brody effect may even diminish R wave amplitude if late activation of the ischemic zone occurs in a tangential manner as previously suggested.²⁶⁾ Also, the Brody effect cannot explain the frequently observed striking transformation of the QRS waveform from an rS wave to an R wave. Although a superimposed Brody effect cannot entirely be ruled out as one of the causative factors in the genesis of the giant R wave, local intramyocardial conduction delay probably plays a more significant role. Furthermore, a discordance between alteration in intracardiac volume and R wave amplitude has been demonstrated during acute myocardial ischemia,²⁷⁾ suggesting that factors other than intravascular volume also determine R wave amplitude. Though further prospective study is necessary, the giant R wave may aid in identifying patients in the very early phase of acute myocardial infarction.

Previously the giant R wave was the subject of a case report¹¹⁾ and therefore, this phenomenon was assumed to occur only rarely. Although it was not the purpose of this study to determine the true incidence and time course of the giant R wave, our results suggest that the giant R wave is not an infrequent finding during the early phase of acute transmural myocardial infarction. In the patients studied the time between the onset of acute myocardial infarction symptoms and the recording of the giant R wave ECG was approximately 2 hours.

CONCLUSION

Our data show the giant R wave occurs together with ST segment elevation and tall T waves in the same ECG leads during the very early phase of acute myocardial infarction. Therefore, appearance of the giant R wave during the early phase of acute myocardial infarction may aid in the ECG diagnosis of acute transmural myocardial infarction and, furthermore, may aid in identifying the very early phase of acute transmural myocardial infarction. The true incidence, time course and clinical significance of the giant R wave of acute myocardial infarction is not yet known. Studies are presently underway addressing these issues.

REFERENCES

1. Pardee HEB: An electrocardiographic sign of coronary artery obstruction. *Arch Intern Med* **26**: 244, 1920
2. Dressler W, Roessler H: High T waves in the earliest stage of myocardial infarction. *Am Heart J* **34**: 627, 1947
3. Brink AJ, Goodwin JF: The precordial T deflection of the electrocardiogram. *Br Heart J* **14**: 331, 1952
4. Hellerstein HK, Liebow IM: Electrical alternation in experimental coronary artery occlusion. *Am J Physiol* **160**: 366, 1950
5. Ekmekci A, Toyoshima H, Kwoczynski JK, Nagaya T, Prinzmetal M: Angina pectoris. V. Giant R and receding S wave in myocardial ischemia and certain nonischemic conditions. *Am J Cardiol* **7**: 521, 1961
6. Prinzmetal M, Kennamer R, Merliss R, Wada T, Bor N: Angina pectoris, I: A variant form of angina pectoris. *Am J Med* **27**: 375, 1959
7. Prinzmetal M, Ekmekci A, Kennamer R, Kwoczynski JK, Shubin H, Toyoshima H: Variant form of angina pectoris: previously undelineated syndrome. *JAMA* **174**: 1794, 1960
8. Schick E, Weiner D, Hood WB Jr, Ryan T: Increase in R-wave amplitude during transient epicardial injury (Prinzmetal type). *J Electrocardiol* **12**: 259, 1980
9. Zemin NA, Rubenfine M, Naini M, Waiszczuk W, Pamatmat A, Cascade PN: Arrhythmias in variant angina pectoris. Relationship of arrhythmias to ST-segment elevation and R-wave changes. *Circulation* **60**: 1343, 1979
10. Gorfinkel AJ, Inglesby TV, Lansing AM, Goodin RR: ST segment elevation, transient left posterior hemiblock, and recurrent ventricular arrhythmias unassociated with pain. *Ann Int Med* **79**: 795, 1973
11. Madias JE: The earliest electrocardiographic sign of acute transmural myocardial infarction. *J Electrocardiol* **10**: 193, 1977
12. Rakita L, Borduas JC, Rothman S, Prinzmetal M: Studies on the mechanism of ventricular activity. XII. Early changes in the RS-T segment and QRS complex following acute coronary artery occlusion. Experimental study and clinical application. *Am Heart J* **48**: 351, 1954
13. Hamlin RL, Pipers FI, Hellerstein HK, Smith R: Alterations in QRS during ischemia of the left ventricular free wall in goats. *J Electrocardiol* **2**: 223, 1969
14. Hamlin RL, Pipers FI, Hellerstein HK, Smith R: QRS alterations immediately following production of left ventricular free-wall ischemia in dogs. *Am J Physiol* **215**: 1032, 1968
15. Holland RP, Brooks H: The QRS complex during myocardial ischemia. An experimental

- analysis in the porcine heart. *J Clin Invest* **57**: 541, 1976
16. Case RB, Nassar MG, Crampton RS: Biochemical aspects of early myocardial ischemia. *Am J Cardiol* **24**: 768, 1969
 17. Regan TJ, Harman MA, Lehan PH, Burke WM, Oldewurtal HA: Ventricular arrhythmias and K^+ transfer during myocardial ischemia and intervention with procainamide, insulin, or glucose solution. *J Clin Invest* **46**: 1657, 1967
 18. Akiyama T: Intracellular recording of in situ ventricular cells during ventricular fibrillation. *Am J Physiol (Heart and Circ Physiol)* **9**: H465, 1981
 19. Hill JL, Gettes LS: Effect of acute coronary artery occlusion on local myocardial extracellular K^+ activity in swine. *Circulation* **61**: 768, 1980
 20. Akiyama T, Richeson JF: The giant R wave of myocardial ischemia (abstr). *Clin Res* **27**: 146A, 1979
 21. Abildskov JA, Klein RM: Cancellation electrocardiographic effects during ventricular excitation. *Circ Res* **11**: 247, 1962
 22. Schaeffer J: Über die absolute Irosse electrocardiograph ischem potentiale. *Pflügers Arch Ges Physiol* **255**: 251, 1952
 23. Brody D: A theoretical analysis of intracavitary blood mass influence on the heart. *Circ Res* **4**: 731, 1956
 24. Millard RW, Hodgkin BC, Nelson C: Effect of ventricular end-diastolic volume on vectorcardiographic potentials of the pig. *Am J Physiol* **235**: H182, 1978
 25. Nelson CV, Chatterjee M, Angelakes ET, Hecht HH: Model studies on the effect of the intracardiac blood on the electrocardiogram. *Am Heart J* **62**: 83, 1961
 26. Voukydis PC: Effect of intracardiac blood on the electrocardiogram. *New Engl J Med* **291**: 612, 1974
 27. David D, Naito M, Chen CC, Michelson EL, Morganroth J, Schaffenburg M: R-wave amplitude variations during acute experimental myocardial ischemia. An inadequate index for changes in intracardiac volume. *Circulation* **63**: 1364, 1981