References


ST-segment Variations after Acute Myocardial Infarction

Relationship to Clinical Status

MARVIN W. KRONENBERG, M.D., MORRISON HODGES, M.D., TOSHO AKIYAMA, M.D.,
DOUGLAS L. ROBERTS, M.D., DENNIS A. EHRC, M.D.,
THEODORE L. BIDDLE, M.D., AND PAUL N. YU, M.D.

With the Technical Assistance of Barbara Zawrotny, Linda Sampson, and Cynthia Murch

SUMMARY  The degree of vectorcardiographic ST-segment elevation was employed as an index of myocardial ischemic injury in a study of 27 patients after acute myocardial infarction (AMI). The ST-segment vector magnitude (STVM) was derived from the continuously recorded modified Frank vectorcardiogram and was plotted serially by hours after onset of AMI. The STVM in normal subjects was 51.1 ± 7.1 μV (mean ± SE). A standard deviation of the pooled variance of 15.2 μV was obtained in a group of control patients and a change of more than 2 SD (> 30 μV) in an individual STVM was considered to be significant. The STVM progressively decreased in patients who survived without clinical complications while it remained elevated in those with congestive heart failure. A modest, sustained re-elevation of STVM was observed in patients who developed pericarditis, and a significant late average increase of 64 μV occurred in survivors with infarct extension. In contrast, STVM underwent a major increase in patients who died. In five of these six patients without associated pericarditis a mean increase of 164 μV was recorded in the last 5–12 hours of life. While death was clinically predictable in two patients with cardiogenic shock, it was not so for the four other patients who died. Thus, major increases in STVM frequently suggested significant new pericardial injury and were often premonitory to sudden death after AMI. The increases preceding death implied that not only ventricular ectopy but also lethal conduction abnormalities after AMI might be ischemia-related.

THERE HAS BEEN recent investigation of the electrocardiographic ST-segment as a quantitative indicator of myocardial ischemic injury. Using multiple lead epicardial and precordial ST-segment mapping techniques, the sum of ST-segment elevations (ΣST) has been employed as an estimate of the extent of myocardial ischemic injury after coronary occlusion in animals and after acute myocardial infarction (AMI) in man. This technique has been used to characterize ST-segment changes in the first two days after AMI in man and employed serially once daily to estimate the frequency of the late infarct extension. Analysis of the ST segment in the standard 12 lead electrocardiogram has shown a strong correlation between major elevation and numerous hemodynamic and arrhythmic complications after AMI.

With each of these electrocardiographic methods data have been obtainable only intermittently, thus limiting the amount of ST-segment information available. Recently we have used a method for continuous recording of the modified Frank X, Y and Z vectorcardiographic (VCG) leads in order to analyze arrhythmias and the ST-segment vector magnitude (STVM). This has allowed for multiple, serial, rapid determinations of STVM, and our previous studies have shown a good correlation between STVM and ΣST obtained from 35 lead precordial maps (N = 51, r = 0.818). We employed this VCG system in a study of patients with AMI in whom we followed serial changes in STVM to characterize what ST-segment alterations were associated with infarct resolution and extension as well as with death after AMI. Normal values for STVM were determined and changes due to pericarditis were examined.

From the Cardiology Unit, Department of Medicine, University of Rochester School of Medicine and Dentistry and Strong Memorial Hospital, Rochester, New York.
Supported in part by Contract NO 1 HV 81331, NIH Training Grant HL 05500, and a Research Training Fellowship 1 F22 HL 01325-01 (RAD) from the NHLI.
Address for reprints: Dr. Marvin W. Kronenberg, Division of Cardiology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232.
Received January 29, 1976; revision accepted May 24, 1976.
Methods and Materials

1. STVM Recording and Measurement

Employing a specially designed cable and amplifier the modified Frank X, Y and Z leads were recorded on a Honeywell 7610 FM magnetic tape recorder at high gain on instrument grade magnetic tape running at 1/2 inches per second. The time of day was continuously encoded with a Systron-Donner time code generator on the tape. The signal-to-noise ratio was 46 dB and the frequency response was flat to 625 Hz. When replayed, X, Y and Z leads were observed on a Tektronix RM 547 oscilloscope and were permanently recorded on a Brush Mark 200 recorder with a deflection of 40 mm/mV. The calibration was checked every 12 hours and was readjusted if necessary, but was constant to within 25 μV, 2% full scale, over spans of one to 10 days.

Each tape was retrospectively replayed to generate permanent records at 8:00 a.m., 4:00 p.m., and 12 midnight, recorded at a paper speed of 100 mm/sec. Other records were made in relation to timed clinical events.

For consistency one investigator analyzed each record using a minimum of three consecutive sinus beats at each point, and one of the authors checked for uniformity of readings. An isoelectric line defined as the TP segment was drawn to connect each beat, and a vertical line was placed at the end of the QRS (J point), detected by finding the last evidence of depolarization in the three leads. At a point 20 msec beyond the end of the QRS complex the deflection of the ST segment in each lead from the isoelectric line was recorded to the nearest one-half mm (12.5 μV). The X, Y and Z values of the three beats were averaged, and the ST-segment vector, azimuth, and elevation were calculated using formulas for their polar coordinates as previously described.10

2. Control Data and Reproducibility

Data from nine healthy subjects (seven men and two women) aged 21 to 62 were used to establish normal values for STVM using this high-gain system. None had early repolarization on the 12 lead ECG.

A group of six patients without cardiac ischemia was monitored continuously for 36-48 hours in order to determine the stability of STVM measurements. Readings were done hourly and occasionally every five minutes for 30-60 minutes for a total of 276 determinations, averaging 46 per subject. A pooled estimate of variance was determined for the group.

Fourteen patients had records of STVM made in four positions in bed to detect postural STVM alterations. Supine, 90° sitting, right and left lateral decubitus recordings were made and the maximum difference in STVM among them in microvolts was recorded.

To evaluate reproducibility between observers, complexes from tapes of another 14 patients were played back twice and two readers separately analyzed identical complexes at 20 and 60 msec after the end of the QRS.

3. The Patient Group

Twenty-seven patients with AMI were studied in the Rochester Myocardial Infarction Research Unit (MIRU). The diagnosis of AMI was made by a typical history of chest pain, classical ECG changes and acute elevations of serum CPK and SGOT. The presence of AMI, sinus rhythm, adequate VCG tapes for analysis, and the absence of bundle branch block were the only criteria for inclusion in this study. Informed consent was obtained for all studies.

Table 1 displays the clinical characteristics of this group of patients. Twenty-six patients had transmural infarcts and one had a subendocardial infarction. Thirteen patients had no evidence of cardiac failure on admission (MIRU Class I) while fourteen had varying degrees of left ventricular failure (MIRU Classes II-IV). Two of the five Class IV patients succumbed during monitoring. Another two died after emergency cardiac surgery. The latter two patients were grouped with the other survivors of the monitoring period for STVM analysis.

Patients were examined frequently and progress described in timed chart notes. The presence or absence of pericardial friction rubs was specifically recorded. Serum LDH, SGOT, total CPK and a 12 lead ECG were obtained daily. Serial hemodynamic monitoring was performed in most patients. One to three VCG leads were displayed for routine rhythm monitoring. Patients were discharged to other areas of the hospital solely on the basis of their clinical progress and without knowledge of trends in STVM.

For each patient STVM was plotted against time after onset of infarction, which was defined as the time of the chest pain which caused the patient to seek medical care. The hospital charts were reviewed, and timed notations of major symptoms, physical findings, and drug therapy were entered on the graphs.

In the nine patients with pericarditis, STVM changes before, during and after this event were examined. Pericarditis was defined by the occurrence of new, anterior pleuritic pain and the presence of a pericardial friction rub.

Eight-hourly changes in STVM after the onset of AMI were determined for the entire group of survivors. When pericarditis developed, the data of such patients were used until new ST-segment elevation with symptoms and signs of pericarditis occurred. Thereafter their data were excluded.

<table>
<thead>
<tr>
<th>Table 1. Clinical Characteristics of MI Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIRU clinical class</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
</tbody>
</table>

Abbreviations: AMI = acute myocardial infarction; A = anteroseptal or anterior; D/L = diaphragmatic or lateral; A+L = anterolateral; A+D = anterior and diaphragmatic; SE = subendocardial.
4. Analysis of STVM Trends

The graphs of the 18 patients without pericarditis (13 alive, 5 dead) were examined to establish the importance of the general trend of STVM over the monitored course and the significance of frequent in-course STVM elevations. The subgroup of nine patients with pericarditis was excluded initially because of the independent influence pericarditis might exert on ST-segment elevation. Significant increases in STVM and the time over which they developed were correlated with survival or death after the increase. STVM determinations were discontinued if bundle branch block occurred. The VCG data and time after onset of AMI for each reading were entered onto punch cards, and a Xerox Sigma 3 computer was used to calculate STVM regression lines by the method of least squares.

The occurrence of congestive cardiac failure was correlated with the level of STVM when the 18 serial plots were arbitrarily divided into groups above and below 100 μV. Seventeen patients could be easily classified into these subgroups.

Data were evaluated by using analysis of variance, Chi square, the Fisher exact probability test, paired and unpaired t-tests, parallel regression, and stepwise discriminant analysis where appropriate.11, 12

Results

1. Control Data

The mean STVM was 51.1 ± 7.1 μV (mean ± SE) for the normal subjects.

The serial STVM readings for a group of patients without cardiac ischemia showed a standard deviation of the pooled variance of 15.2 μV, and this was very close to the precision of the manual-visual measuring system employed. Thus, a change of more than 30 μV (2 standard deviations) was considered to be significant.

The postural data showed a mean maximal difference in STVM among the four positions tested of 23.5 ± 5.3 μV; the range of values was 4–38 μV among 13 subjects, although a single patient showed a postural change of 82 μV. No position was consistently associated with a greater STVM than the others.

There was no significant difference between two observers measuring the same ST segments 20 msec as well as 60 msec after the end of the QRS.

2. Patients with Acute Myocardial Infarction

Twenty-one patients survived and six died during the monitoring period.

Among the 21 survivors, 14 showed a decrease or no change in STVM while seven had some increase in the final STVM compared to the initial values. Figure 1 displays the mean serial eight-hourly STVM of all survivors and of those patients initially without complication (Class I). For the entire group there was little change in the mean STVM over their monitored course, but when divided by clinical status on admission, patients without complication tended to have a progressive decline in STVM, returning to the normal range by 86 hours, while the STVM of survivors with congestive cardiac failure tended to remain above normal. The 11 patients without pericarditis who had serial tracings persistently above 100 μV had a greater incidence of congestive cardiac failure than did the six below that level (P = 0.03).

Seven survivors had an increase in the final STVM. Of the six without pericarditis, three with probable infarct extension averaged 64 μV over admission values. The remaining three survivors had small STVM increases, averaging only 29 μV, without satisfactory explanation. No survivor had known infarct extension without an increase in STVM.

Nine patients with pericarditis had an initial downward trend in STVM followed by a new elevation of the STVM curve which then gradually decreased over the course of several days. Seven had a decrease or no change in the initial vs final STVM. One patient who died had a marked terminal increase in STVM, and the remaining one patient, who had an evolving infarction, had a markedly fluctuating STVM. Thus, even in the presence of pericarditis, without other complications the final STVM tended to be the same or less than the admission value when the signs of pericarditis had resolved.

In contrast to the predominantly downward course of survivors, the STVM of the patients who died showed a significant degree of secondary rise (fig. 2). Five of the six patients had generally high STVM values compared to the mean for survivors. Patient P.A. developed pericarditis. Although death was clinically likely in the two patients with cardiogenic shock, the clinical status of the other four patients was actually improved or unchanged. Thus, death was sudden and clinically unexpected in four of the six patients, but STVM rose before death in all six.

The preterminal increases in STVM among the fatal group were followed by arrhythmias and conduction disturbances. Ventricular tachyarrhythmias occurred in two patients, atrioventricular (A-V) block and bundle branch block in two, acute left anterior hemiblock (LAHB) in one, and asystole in one. In each case these changes were followed by circulatory collapse and death after unsuccessful
resuscitative efforts. Figure 3 displays preterminal ischemic ST-segment changes in E.M., who had a subendocardial infarction. STVM continued to rise although remarkable clinical improvement had occurred during a continuous nitroprusside infusion. AT 88.6 hours after onset there was further ST-segment depression in lead X and STVM rose to 412 μV associated with further hemodynamic alterations. Three minutes later STVM rose to 594 μV and ventricular tachycardia occurred.

Postmortem examination in five of the six patients who died confirmed the presence of severe coronary artery disease with extensive myocardial infarction. Myocardial rupture occurred in one patient and severe left ventricular free wall softening in another. Serial sections of the conduction system in the hearts of four patients failed to show ischemic damage to these structures.

Quantitative analysis of STVM fluctuations was done and there were significant differences in the tracings of the 18 patients without pericarditis when divided by clinical status. For the entire monitored course the 13 survivors showed a drop of 12 ± 18 μV while the five who died had an increase of 184 ± 61 μV. The ten survivors without infarct extension had a mean decrease in STVM of 34.3 μV compared to an increase of 64 μV in the three with extension.

In the patients without pericarditis there were 32 significant in-course rises in STVM with survival compared to the five final elevations of the patients who died. The major increase in STVM of the five patients who died occurred in the last 5–12 hours of life. Their STVM rose 164 μV compared to an increase of only 8 μV for survivors at an equal time after onset of AMI. Of the five preterminal slopes one was slow, two were moderately fast and two were very fast rises; they ranged from 0.1 to 24.7 hours in duration. Stepwise discriminant analysis disclosed that both the change in magnitude and the slope of the rises in STVM were important factors in classifying patients into alive or dead groups. A change in magnitude was more important than a change in slope, and the actual time required to inscribe the change was not significant. Slope added little to the predictive ability in this small group. Based upon these findings, an increase in STVM greater than 150 μV was considered to be of predictive value for imminent death (F₁,₃₀ = 11.32, P<0.01). Using this criterion we evaluated the frequency of STVM fluctuations in the entire population, both with and without pericarditis. In spite of the general elevation of STVM due to pericarditis, there was no apparent difference in the frequency and extent of STVM fluctuations between those with and without this process. There were 12 major increases (>150 μV). These occurred in only eight of 27 patients, and four of these eight died soon after the increases occurred. Conversely, only four of 21 survivors experienced major increases in STVM. These four patients had angina, evolving MI, pericarditis, and congestive cardiac failure, respectively. Eighty-three percent of all major increases were associated with clinical ischemic or fatal events.

The numerous smaller but significant fluctuations in STVM were not always correlated with significant clinical events.

**Discussion**

The serial STVM readings in the nonischemic subjects proved to be quite stable. However, two-thirds of the MI patients had one or more significant re-elevations of STVM during the monitored course, suggesting prolonged susceptibility to intermittent ischemia after AMI. While frequently correlated with clinical events capable of provoking ischemia, not all such fluctuations were associated with these findings. Thus, in addition to obvious clinical insults, there may have been less evident causes of ST-segment elevation.
after AMI. Both subclinical ischemia and undetected pericarditis are possible explanations for these findings. The former may be more likely because of the relatively transient nature of these re-elevations. We concluded that, in patients with AMI, a progressive decrease in STVM without significant secondary rise usually indicated a favorable prognosis. Secondary rises were associated with pericarditis, angina without re-infarction, sequelae of atrial or ventricular tachyarrhythmias, infarct extension or impending death.

The magnitude of the increases in STVM suggested that large increases in STVM (>150 μV) might be a quantitative expression of severe, potentially lethal ischemic injury. Four of the six fatal patients had such large increases in STVM. No survivor in the group with extension of infarction had an increase in STVM of that magnitude. Exceptions to the predictive value of the STVM were observed, but in survivors after excluding pericarditis, there were few instances of such increases, and transient ischemia was frequently the cause.

The possibility of rather frequent, but sometimes subclinical, myocardial ischemia reflected by changes in precordial ST mapping has been mentioned in several reports. Reid and his associates studied a group of 19 patients with AMI using daily precordial ST-segment maps and found that 12 of 14 patients with transmural infarction had late increases in 2ST; eight of these 12 patients (66%) had re-elevation of serum CPK as well, reflecting infarct extension. Reese and co-authors found wide variability in 2ST after AMI, and noted that re-elevations were not always associated with infarct extension.\textsuperscript{18} Madias et al.,\textsuperscript{5} who studied 37 patients with AMI, found evidence for infarct extension in 18. One patient with subendocardial ischemia had a progressive increase in ST depression, evolved an anterior transmural MI and died in cardiogenic shock. This finding of progressive ischemic ST-segment change prior to major myocardial damage is similar to the results we report in this paper.

In the presence of persistent major ST-segment elevations in the 12 lead ECG after AMI, studies by Wilson and Pantridge\textsuperscript{3} and by Nielsen\textsuperscript{4} disclosed a significantly higher incidence of late ventricular dysrhythmia. Other studies have also shown an increase in ventricular extrasystoles after infarct extension\textsuperscript{14} and A-V block with ischemic ST-segment elevation.\textsuperscript{18} Sutton and Davies\textsuperscript{26} have correlated necrosis of the bundle branches with acute infarction of the interventricular septum. Alonso and associates\textsuperscript{27} and James\textsuperscript{28} have detected ischemic atrial damage in patients with MI having atrial arrhythmias.

In our patients who died, after major STVM rise two patients developed ventricular tachyarrhythmias, two had A-V block and bundle branch block, one had LAHB with perforation of the left ventricle, and one developed asystole. We postulate that the mechanism of sudden death in these patients may well have been further ischemic injury to the myocardium and the specialized conduction system. The preterminal increases in STVM may implicate further ischemic injury as the cause of such sudden deaths several days after AMI.

Added support for this concept comes from clinical studies of patients without AMI who have also documented arrhythmias and conduction disorders in the presence of ischemic ST-segment changes. Gorfinkel and associates\textsuperscript{29} described a patient who developed both ventricular tachycardia and left posterior hemiblock with ST-segment elevation. Similarly, Lasser and de la Paz\textsuperscript{26} documented the occurrence of complete A-V block with ischemic ST-segment elevation of the Prinzmetal type.

In conclusion, the continuously recorded Frank VCG provided useful information about the ST segment after AMI. A major increase in the STVM was often an ominous sign in the small group studied. If confirmed in future studies, this parameter might allow an objective index of risk to be applied to a group of patients with AMI who, although seriously ill, could not be clinically predicted to be at imminent risk of sudden death. The potential exists for the development of an electrocardiographic warning system to detect these ST-segment alterations.

Acknowledgment

The authors thank Eric A. Schenck, M.D. for his investigation of the conduction system in the hearts. The able assistance of MIRU technicians Frederick A. Eames, John R. Chance, Arthur Salo, Thomas Craine and Dwain Wilder is gratefully acknowledged. We are grateful to Mrs. Margaret Mecredy for statistical analyses and to Miss Sharon Frederick and Mrs. Summer King for their secretarial assistance.
Reduction of Ischemic Injury by Sublingual Nitroglycerin in Patients with Acute Myocardial Infarction

Najam A. Awan, M.D., Ezra A. Amsterdam, M.D., Zakauddin Vera, M.D., Anthony N. Demaria, M.D., Richard R. Miller, M.D., and Dean T. Mason, M.D.

SUMMARY The effect of sublingual nitroglycerin (NTG) on myocardial ischemic injury was evaluated in eleven patients with acute anterior myocardial infarction. Precordial 35-lead ST-segment maps were obtained in each patient immediately before and 3-10 minutes after 0.4 mg sublingual NTG. The following measurements were made from each ST map: N-ST, ST (number of leads showing ST elevation > 1 mm), S (total ST elevation in all leads), ST (average ST-segment elevation in those leads with > 1 mm elevation). Following 0.4 mg sublingual NTG evidence of myocardial ischemic injury as assessed by ST-segment mapping decreased in association with reduction of heart rate × systolic blood pressure product (10.80 × 108 to 9.49 × 108, P < 0.001). Group mean values diminished significantly for N-ST (18.1 to 14.4, P < 0.001), S (37.9 to 30.1, P < 0.005) and ST (1.7 to 1.4, P < 0.001). Evaluation performed by the technique of precordial ST-segment mapping suggests that sublingual nitroglycerin in a commonly employed clinical dose is associated with evidence of reduced ischemic cardiac injury in patients with acute myocardial infarction. This effect appears to be related to reduction of myocardial oxygen demand by the nitrate.

CURRENT UNDERSTANDING of the pathophysiology of myocardial infarction has resulted in recent emphasis on therapeutic manipulation of the determinants of myocardial oxygen consumption (MVO2) in order to reduce myocardial ischemia and decrease injury.1-3 Since the complications and mortality of acute myocardial infarction are closely related to extent of cardiac damage,4 the limitation of ischemic injury in this setting. Nitroglycerin (NTG) is considered to exert its beneficial clinical effects in angina pectoris by reduction of MVO2.5-9 suggesting its potential for reduction of ischemic injury in myocardial infarction by a similar action. Studies of the effects of NTG on cardiac function have demonstrated decrease in ventricular dimensions and blood pressure,10-12 major determinants of MVO2. More recently our group13, 14 and others15, 16, 17 have shown similar beneficial hemodynamic results in patients with acute myocardial infarction.

Precordial ST-segment mapping as developed by Maroko and associates1-3 has been utilized to quantitatively assess...
ST-segment variations after acute myocardial infarction. Relationship to clinical status.
M W Kronenberg, M Hodges, T Akiyama, D L Roberts, D A Ehrich, T L Biddle and P N Yu

Circulation. 1976;54:756-761
doi: 10.1161/01.CIR.54.5.756

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1976 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/54/5/756

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/