VECTORCARDIOGRAPHIC CHANGES DURING INTRACORONARY INJECTIONS

By Raphael F. Smith, M.D., J. Warren Harthorne, M.D., and Charles A. Sanders, M.D.

SUMMARY
To determine mechanisms of myocardial toxicity of radiopaque media and to correlate specifically induced changes in the composition of coronary artery blood with changes in the surface electrocardiogram, simultaneous recordings were made from Frank leads X, Y, and Z during intracoronary injections of radiopaque media and special test solutions. The study group consisted of 19 patients, 29 to 64 years of age, with either abnormal or normal-appearing coronary vessels on cineangiography. Recordings were analyzed with an electronic integrator, an oscilloscope, and directly from photographic tracings.

With injections of sodium-containing radiopaque media into the right coronary system, the spatial mean T vector increased in magnitude and deviated to the left and superiorly. With injections into the left coronary system, the T vector increased in magnitude and shifted to the right, downward, and anteriorly. Changes in the QRS complex were less constant but, when present, consisted of slight prolongation of the QRS duration and shift of the QRS vector toward the area of myocardium perfused by the coronary system injected.

Similar T-vector changes could be produced by intracoronary injections of saline solutions, but minimal or no changes were observed with injections of hypertonic mannitol, Ringer's solution, hypoxic blood, plasma, and 5% dextrose in water.

It is concluded that the T-wave changes are caused by regional prolongation of the repolarization process, presumably due to extracellular sodium excess or sodium-calcium antagonism. Delay of the repolarization process and the resulting potential difference may be responsible for re-entrant excitation and the ventricular arrhythmias observed during coronary angiography.

Additional Indexing Words:
Electrocardiographic changes  Vectorcardiographic analysis
Electrophysiology  Coronary arteriography

Profound alterations of the electrocardiogram (ECG) occur during coronary angiography and have been qualitatively described for single ECG leads1-5 and for the limb leads. In addition to changes in configuration of the electrocardiogram, arrhythmias arise and a decrease in the contractile force of the heart has been observed during intracoronary injections of contrast material.4 In previous reports it has been postulated that the cardiovascular effects are due to a toxic action of the radiopaque agent5-8 or specifically to the hypertonicity of the medium,9 while other investigators have suggested that the cardiovascular alterations are the result of ischemia produced by the displacement of coronary arterial blood by contrast material.4 Coronary angiography is being used in clinical evaluations with increasing frequency, and further elucidation of the mechanisms of myocardial toxicity is needed.

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Opinions or conclusions contained in this paper are those of the authors and do not necessarily reflect the views or endorsement of the Navy Department.
From observation of the electrocardiogram during angiography, it became apparent to us that selective injection of a coronary artery during an angiographic study is a means of altering the composition of the arterial blood perfusing a region of myocardium, and that basic electrophysiological information could be obtained by correlating the changes in the surface electrocardiogram with the specific intervention carried out. The purpose of this report is to present a detailed vectorcardiographic analysis of ECG changes during intracoronary injections of contrast material and of other test solutions; to resolve the question of whether the ECG changes are due to ischemia, hypertonicity, or the ionic composition of the injectate; and to propose a mechanism to explain the genesis of the ventricular arrhythmias and the ECG changes from observations of the surface electrocardiogram during coronary injections.

**Methods**

Nineteen patients, 12 men and seven women, who ranged in age from 29 to 64 years and were referred to the Cardiac Catheterization Laboratory for selective coronary cineangiography, were studied. A coronary angiographic study was indicated either for evaluation of atypical chest pain or for evaluation of the coronary circulation prior to cardiac surgery. The patients were premedicated with meperidine (50 mg). The Frank lead system\(^6\) was applied, and the electrodes were held in place by patches of elastic tape. Prior to the injection of contrast material, control tracings were taken simultaneously from three orthogonal leads. Under local anesthesia with lidocaine, a no. 7.5 Sones catheter was introduced into the brachial artery and advanced to the root of the aorta. The catheter was positioned in the ostium of the coronary artery to be studied. Cineangiograms were made by using Hypaque-M 90 (sodium diatrizoate 30%, methylglucamine diatrizoate 60%) diluted with saline to provide a 69% solution of Hypaque, or Renovist (sodium diatrizoate 35%, methylglucamine diatrizoate 34.3%). The volume of contrast material injected ranged from 6 to 8 ml.

During a control period prior to injection and during the subsequent injections of the coronary arteries, scalar tracings were recorded on a Sanborn 350 photographic recorder. An Ampex FR 1300 magnetic tape recorder was used to record the three scalar leads during studies of six patients. The area of the electrocardiogram was measured electronically\(^1\) from the tracings recorded on magnetic tape, and vectorcardiographic parameters were calculated by digital computer. Vector analysis of 13 photographic records was accomplished by measuring the peak amplitude of the QRS and T waves and using this value in the spatial trigonometric computations. If the waveform was biphasic, net amplitude was used. Instantaneous vector loops were displayed on a Sanborn 569 oscilloscope and photographed with a Polaroid camera.

In addition to the injections of angiographic contrast material, special test solutions were introduced through the catheter into the main right and left coronary arteries. Prior to injecting the test material, it was necessary to visualize the

### Table 1

**Physical Characteristics of Solutions Injected**

<table>
<thead>
<tr>
<th>Injectate</th>
<th>Approximate sodium concentration (mEq/L)</th>
<th>Approximate osmolarity (M osm/L)</th>
<th>Other constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renovist</td>
<td>600</td>
<td>1800</td>
<td>Sodium diatrizoate 35%; methylglucamine diatrizoate 34%</td>
</tr>
<tr>
<td>Hypaque 69%</td>
<td>400</td>
<td>1700</td>
<td>Sodium diatrizoate 35%; methylglucamine diatrizoate 34%</td>
</tr>
<tr>
<td>0.9% Saline</td>
<td>154</td>
<td>350</td>
<td></td>
</tr>
<tr>
<td>2% Saline</td>
<td>325</td>
<td>620</td>
<td></td>
</tr>
<tr>
<td>3% Saline</td>
<td>513</td>
<td>950</td>
<td></td>
</tr>
<tr>
<td>Ringer's solution</td>
<td>130</td>
<td>280</td>
<td></td>
</tr>
<tr>
<td>Dextrose, 5% in water</td>
<td>280</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma</td>
<td>140</td>
<td>280</td>
<td></td>
</tr>
<tr>
<td>Coronary sinus blood</td>
<td>140</td>
<td>280</td>
<td></td>
</tr>
<tr>
<td>Mannitol, 5%</td>
<td>140</td>
<td>280</td>
<td></td>
</tr>
<tr>
<td>Mannitol, 15%</td>
<td>140</td>
<td>280</td>
<td></td>
</tr>
</tbody>
</table>

*25% Oxygen saturation.
Figure 1

Changes in scalar complexes with intracoronary injections of contrast agent in a 33-year-old man in whom no heart disease was detected. The tracings are simultaneously recorded from Frank leads X, Y, and Z. The marker at the bottom of the record indicates the end of the injection. The negative sign (preceding) Z denotes that the back electrode is negative, a departure from Frank lead convention.
coronary tree with a small amount of contrast material. The catheter was then flushed, and the electrocardiogram was allowed to return to its preinjection configuration before the test solution was given. The following solutions were used: 0.9% sodium chloride; 2% sodium chloride; 3% sodium chloride; 5% dextrose in water; lactated Ringer's solution, autologous heparinized plasma, autologous heparinized coronary sinus blood; and 5% and 15% mannitol. Physical characteristics of these solutions are contained in table 1. These solutions were chosen to assess the effect on the vectorcardiogram of increasing the sodium concentration, of tonicity, of lowering oxygen tension, and of displacing coronary artery blood with a nonoxygenated solution. Venous blood and dextrose in water, administered to experimental animals in a previous study showed minimal or no electrocardiographic effect, and the concentration of sodium in the sodium chloride solutions we used did not exceed that present in radiopaque media which have been safely used in selective coronary angiography.

In two of the patients, brachial blood pressure was measured continuously with a Statham P23Db transducer during the injections.

**Results**

**Intracoronary Injections of Contrast Agents**

The duration and configuration of the T waves of each patient changed with injections of contrast material (Hypaque 69% and Renovist) into the left (LCA) and right (RCA) coronary artery systems. In seven patients with radiographically normal coronary arteries, LCA injections resulted in prolongation of the scalar T waves, a transient increase in the spatial magnitude of the mean T vector, and deviation of the vector to the right, anterior, and downward. In the same patients, RCA injections of contrast media produced an increase in the magnitude of the spatial T vector, prolongation of the scalar T waves, and a spatial mean T vector that was directed to the left and upward. There was a variable change of the T wave of lead Z in the group of seven patients with normal coronary arteries; five members of the group exhibited an anterior shift in the mean T vector with RCA injection, and two members of the group had posterior deviation of the mean T vector. Figure 1 depicts scalar ECG changes recorded simultaneously from Frank leads X, Y, and Z during RCA and LCA injections of Hypaque 69%. Mean vector items computed from electronic analysis of the magnetic tapes recorded on six subjects appear in table 2. Photographic records of X, Y, and Z scalar tracings were made during the remaining 13 studies, and mean vector items

![Spatial mean T-vector direction with right (RCA) and left (LCA) coronary artery injections of contrast material. An orthogonal reference system is used with z axis perpendicular to the page. Two patients with left bundle-branch block are not included in the diagram but are discussed in the text.](Downloaded from http://circ.ahajournals.org/ by guest on January 15, 2018)
Table 2

Comparison of Mean Vectorcardiographic Items During Intracoronary Injections

<table>
<thead>
<tr>
<th>Injectate</th>
<th>Magnitude (µV-sec)</th>
<th>Direction (°)</th>
<th>Spatial angle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aQRs</td>
<td>aT</td>
<td>eQRs</td>
</tr>
<tr>
<td>Control</td>
<td>26</td>
<td>44</td>
<td>66</td>
</tr>
<tr>
<td>RCA Hypaque</td>
<td>32</td>
<td>84</td>
<td>111</td>
</tr>
<tr>
<td>LCA Hypaque</td>
<td>55</td>
<td>149</td>
<td>118</td>
</tr>
<tr>
<td>Control</td>
<td>23</td>
<td>25</td>
<td>47</td>
</tr>
<tr>
<td>RCA dextrose</td>
<td>25</td>
<td>25</td>
<td>49</td>
</tr>
<tr>
<td>RCA Ringer’s solution</td>
<td>26</td>
<td>32</td>
<td>55</td>
</tr>
<tr>
<td>Control</td>
<td>18</td>
<td>40</td>
<td>49</td>
</tr>
<tr>
<td>LCA hypoxic blood</td>
<td>22</td>
<td>23</td>
<td>31</td>
</tr>
</tbody>
</table>

Patient 24: female, age 61 yr; normal LCA system; focal lesion of RCA with partial occlusion

Patient 22: male, age 45 yr; normal LCA system; focal lesion mid-RCA with almost complete occlusion

Patient 10: female, age 29 yr; normal RCA and LCA systems

Patient 23: male, age 34 yr; intimal irregularities of LCA system with total occlusion mid-RCA

Patient 13: male, age 47 yr; total occlusion of left anterior descending artery; mild intimal disease of RCA system

Patient 25: female, age 36 yr; juvenile onset of diabetes, LBBB, heart failure, diminutive vessels throughout RCA and LCA systems
were calculated from maximum scalar amplitudes (see "Methods"). Figure 2 is a composite diagram which illustrates the shift in mean T vector with RCA and LCA injections of contrast media. It can be seen that, with RCA and LCA injections, T vectors become oppositely directed in the spatial reference system. Typical instantaneous vector loops are shown in figure 3 A to D. The directional changes in the spatial T-vector loop with RCA and LCA injections are similar to the changes noted in the mean vector direction. The magnitude of the response to the injection was conditioned by the patency of the coronary system into which injection was made and by the volume of the contrast agent delivered to the coronary artery. There was less response to the injection when occlusive disease of the coronary system was present.
or when part of the injectate refluxed from the coronary ostium into the aorta.

The spatial ventricular gradient (G) changed in the same direction as the mean T vector with both RCA and LCA injections in five of the six records analyzed with the electronic integrator. The exception was noted in a 36-year-old female with left bundle-branch block (patient 25) whose record showed prolongation of the QRS duration with RCA and LCA injections and decrease of the T-vector magnitude. The deviation of the spatial G vector was concordant with the spatial QRS vector change in this patient. A second patient with left bundle-branch block had responses to LCA and RCA injections of contrast media that were similar to the typical vector changes although his pre-injection QRS and T-spatial vectors were grossly abnormal.

Changes in the QRS complex were less marked and constant than the T-wave changes in 18 of the 19 patients. In each patient exhibiting a QRS vector change, there was an increase in the QRS duration. This increase did not exceed 20 msec in any patient. On
Figure 4

Changes in scalar complexes with sodium chloride injections of different concentrations in a 40-year-old male. Occlusive disease was present in both RCA and LCA systems.
the scalar records, the most common response to LCA injections was an increase in the peak QRS amplitude on lead X, and decrease of the peak QRS on leads Y and Z.
The maximum instantaneous vector increased in essentially the same direction as the maximum QRS vector of the control loop (fig. 3A and C). The electronically derived spatial mean QRS vectors of the patients without bundle-branch block showed a slight increase in magnitude in four patients and a slight decrease in one. With RCA injections of contrast media the spatial vector loop became more inferiorly oriented, with the largest change occurring in the terminal 20-msec portion of the loop (fig. 3B and D). The terminal vectors increased in magnitude and shifted to the right, posterior, and downward. Scalar QRS complexes typically showed a decrease in peak amplitude on lead X and an increase in lead Y. The response on lead Z was variable.

**Intracoronary Injections of Saline**

The spatial mean T-vector orientation with saline injections (sodium chloride, 0.9, 2, and 3%) was similar to the T-vector changes described with RCA and LCA injections of contrast media. The degree of the change, both in direction of the vector and the size of the vector, was a function of the concentration of the sodium chloride in the injectate. Although typical T changes were noted with saline injections, QRS changes similar to those observed with contrast material were not noted. Figure 4 shows the typical progression of T changes as the concentration of sodium chloride is increased during a series of RCA and LCA injections.

**Intracoronary Injections of Other Test Solutions**

Intracoronary injections made with lactated Ringer's solution (13 injections), 5% dextrose and water (four injections), hypertonic mannitol (six injections), autologous heparinized plasma (two injections), or autologous heparinized coronary sinus blood (three injections) produced minimal or no change in the vectorcardiographic items.

**Arrhythmias Noted with Intracoronary Injections**

Sinus bradycardia was the most common arrhythmia observed during intracoronary injections. In patients with normal-appearing left and right coronary arteries, slowing of rate was noted during both RCA and LCA injections. The degree of slowing was roughly proportional to the amount of contrast agent delivered to the coronary system and, with saline injections, was related to the concentration of sodium chloride in the injectate. There was no response or it was modified when there was occlusive disease of the arterial system injected. One patient (patient 24) had extreme bradycardia during RCA injections; atropine sulfate 0.5 mg was
administered intravenously, and the bradycardia did not recur. In two patients with pre-existing atrial fibrillation, no change in the average R-R interval occurred with LCA injections. With RCA injections, the mean R-R interval increased in both patients, but this change was not statistically significant when the pre-injection beat-to-beat variation was considered.

Transient runs of ventricular tachycardia were seen in three patients: (1) following RCA injection of Hypaque 69% (patient 18); (2) after LCA injection of Hypaque 69% (patient 10); and (3) after injection of 3% saline into the RCA system (patient 25). In each patient the arrhythmia spontaneously reverted to sinus rhythm after a few seconds. Simultaneously recorded orthogonal leads showing the onset of ventricular tachycardia appear in figures 5 and 6. In each case a premature ventricular beat during the prolonged T wave presaged the onset of ventricular tachycardia. In a fourth patient, a slower ventricular ectopic arrhythmia and transient atrioventricular dissociation occurred with LCA injection of Hypaque 69%.

**Discussion**

The prolongation of the T wave with the injection of radiopaque media and the deviation of the ventricular gradient vector away from the area of myocardium, primarily perfused by the arterial system into which injection was made, strongly suggest that this intervention produces regional delay of the repolarization process. Prolongation of the repolarization process by cooling the lateral wall of the right ventricle produces T-wave changes similar to those resulting from our RCA injections, and cooling the lateral left ventricular wall produces changes resembling those from LCA injections. Minor changes in the duration of the QRS complex and QRS vectors (usually deviation toward the region injected) indicate that the depolarization process is affected but to a lesser degree. The effects of intracoronary injections have been noted repeatedly to be related to

![Figure 5](image-url)

**Figure 5**

Ventricular tachycardia during RCA injection of Hypaque 69% in a 46-year-old female with moderate rheumatic heart disease but radiographically normal coronary arteries. The arrhythmia was of brief duration.
the volume of contrast medium that reaches the myocardium, and occlusive coronary disease may decrease the changes associated with injections or cause paradoxical responses due to obstruction to the usual course of flow with retrograde filling from the other coronary system.5

With injections of sodium chloride solutions, similar changes in the repolarization wave and similar alterations of the cardiac rhythm were noted. These changes were not seen with sodium-free solutions of equal osmolarity and with injections of substances that would be expected to displace oxygenated blood. These observations are interpreted as indicating that the ECG changes are largely due to sodium ion rather than to ischemia or hypertonicity. Although sodium chloride solutions produced changes very similar to those occurring with radiopaque agents, the changes were not so marked and alterations of the QRS were not observed. In the two patients in whom brachial artery pressure was measured during injections, the systolic blood pressure regularly fell 5 to 10 mm Hg during injections with contrast media and saline solutions, which is consistent with the negative inotropic effect noted previously with sodium-containing radiopaque agents.4 In support of the contention that the specific ionic composition of the medium is an important factor in the toxicity, Guzman and West13 noted that intracoronary injections of sodium-containing radiopaque agents produced cardiac arrhythmias, ECG effects, and depression of contractility with greater frequency than low-sodium media or sodium-free media. Gensini and DiGiorgi7 also concluded, from studies on experimental animals, that the sodium ion (or the protective effect of methylglucamine salts) was an important factor in the myocardial toxicity of radiopaque media.

Prolongation of the plateau of the cardiac action potential is the electrophysiological effect of increasing extracellular sodium.14 In the frog's heart, increasing the sodium concentration of the perfusing bath reduces the contractile strength of twitches and contractions.15 Luttgau and Niedengerke15 have described competitive antagonism between sodium ion and calcium ion and postulate that there is competition at the cell surface for a negatively charged substance. Since prolongation of the repolarization process and arrhythmias can be produced by acutely lowering myocardial calcium with chelating agents in experimental animals,16 it is attractive to speculate that the electrophysiological and negative inotropic effects noted with intracoronary injections of sodium chloride and sodium-containing contrast agents are

Figure 6
Ventricular tachycardia occurring with LCA injection of Hypaque 69% into a 29-year-old female in whom no heart disease was detected. The arrhythmia was self-limited.
due to sodium-calcium antagonism. There is indirect evidence of this relationship since the addition of calcium and magnesium ions to a solution of sodium metrizoate increases the LD₅₀ in the rabbit.* A greater ECG effect was noted with sodium-containing contrast agents than with solutions of sodium chloride. Prolongation of the action potential has been observed in experimental animals when chloride was replaced by anions to which the membrane is less permeable.¹⁷ Diatrizoate, the primary anionic constituent of Hypaque and Renovist, would be expected to cause a similar response.

The mechanism of regional prolongation of the repolarization process is possibly operative in the production of the ventricular arrhythmias associated with coronary angiography. Delay of repolarization in an area of the myocardium could cause potential differences between adjacent regions and initiate premature beats by reentrant excitation. This mechanism is considered to be of importance in the genesis of cardiac arrhythmias.¹⁸ The three patients in whom ventricular tachycardia developed had prolongation of the T wave prior to the onset of tachycardia, and the appearance of a premature ventricular beat presaged the onset of ventricular tachycardia in all three. Long sinus pauses frequently occurred during coronary artery injections, but ventricular escape beats were not observed.

Sinus bradycardia was frequently noted with both RCA and LCA injections. Other investigators have attempted to relate the presence of sinus slowing to the coronary artery injected as a means of determining the origin of the blood supply of the sinus node.⁵ An increase of sodium inward current or sodium-calcium antagonism should cause lowering of the threshold for firing of pacemaker cells and enhance automaticity.¹⁴ On the other hand, delay of repolarization may result in slowing of pacemaker firing. Our data do not provide specific information pertaining to the mechanism of sinus bradycardia with intracoronary injections.

*Data supplied by Nyegaard & Co., Oslo, Norway.

Conclusions

Vector analysis of the T-wave changes associated with intracoronary injections of radiopaque media and saline solutions indicates that there is prolongation of the repolarization process in the areas of the myocardium primarily perfused by the coronary system into which injection is made. Although QRS changes were inconstant and less marked than the T-wave changes, the data suggest that the depolarization process is also prolonged with injections of contrast material.

The T-wave changes and ventricular arrhythmias observed during this study are primarily due to an electrophysiological effect of the contrast material rather than to ischemia secondary to displacement of oxygenated coronary arterial blood or to the hypertonicity of the medium. The similarities between the effects of sodium chloride solutions and contrast media are presumptive evidence that the sodium ion (or calcium antagonism by sodium) is an important factor in the myocardial toxicity of radiographic agents. Regional delay of repolarization may initiate premature beats and re-entrant excitation by establishing adjacent areas of potential differences. This mechanism is consistent with observations of ventricular arrhythmias during this study.

References


Vectorcardiographic Changes During Intracoronary Injections
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