Ventricular Sensory Endings Mediate Reflex Bradycardia During Coronary Arteriography in Humans

James A. Arrowood, MD, Pramod K. Mohanty, MD, John McB. Hodgson, MD, Mark E. Dibner-Dunlap, MD, and Marc D. Thames, MD

It has been suggested that the response to the intracoronary injection of radiographic contrast is reflex in origin and results from stimulation of ventricular sensory endings. Cardiac transplantation results in denervation of the ventricles, and thus, may interrupt the afferent limb of this reflex. In contrast, the recipient sinus node and atrial remnant remain innervated, leaving the efferent cardiac limb of this reflex intact. We hypothesized that if contrast-induced reflex bradycardia and hypotension occurred from stimulation of ventricular chemosensitive endings, then this response would be abolished after cardiac transplantation. To test this hypothesis, we determined the changes in recipient (innervated) and donor (denervated) sinus-node rates (SNR) and mean arterial pressure during selective right (RCA) and left coronary artery (LCA) injection during arteriography in cardiac transplant patients and in patients with intact cardiac innervation. An increase in the recipient SNR was observed in cardiac transplant patients during left and right coronary injections (LCA, 6.6±1.7 beats/min; RCA, 2.4±1.4 beats/min) compared with a decrease in the control subjects (LCA, -15.3±2.3 beats/min; RCA, -6.9±1.9 beats/min; p<0.05 vs. control). This occurred despite significant and comparable decreases in mean arterial pressure in cardiac transplant patients (LCA, -12.7±2.3 mm Hg; RCA, -11.4±2.2 mm Hg) and control subjects (LCA, -18.7±1.7 mm Hg; RCA, -10.7±1.6 mm Hg). The donor SNR slowed for LCA injection (-5.4±2.1 beats/min, p<0.05) and RCA injection (-3.0±1.7 beats/min), which, for the LCA, was less than the slowing of control subjects (p<0.05). The responses of the denervated donor sinus node were due to a direct chemical (nonneurogenic) effect of radiographic contrast, whereas the increases in the recipient SNR were mainly due to arterial baroreflex activation secondary to the decrease in mean arterial pressure. Our results suggest that the net responses to coronary arteriography in subjects with intact innervation are the result of the integration of ventricular reflexes mediated by chemosensitive endings, arterial baroreflexes, and direct effects of contrast on the sinus node. (Circulation 1989; 80:1293-1300)

Previous work in animals has shown that there are sensory endings in the heart that can be activated by mechanical and/or chemical stimuli. Stimulation of some of these endings subserved by vagal afferents results in reflex vagal-efferent activation and sympathetic withdrawal leading to bradycardia, vasodilation, and hypotension.

Mechanosensitive endings are activated by the mechanical activity of the heart,1,2 and chemosensitive endings are activated by a variety of chemical agents including radiographic contrast agents, capsaicin, and prostaglandins.3-5 Endings are located throughout the cardiopulmonary region; however, in animals, responses are most marked when left ventricular endings are stimulated.

In humans, bradycardia and hypotension have been observed during inferoposterior myocardial infarction6 and coronary arteriography.7-9 It has been postulated that these responses also are reflex mediated through stimulation of ventricular sensory endings similar to the ones described in animals. In previous studies,7-9 it has not been possible to test this hypothesis directly because this would require selective interruption of ventricular afferents. More-
TABLE 1. Clinical Characteristics and Baseline Values

<table>
<thead>
<tr>
<th></th>
<th>Control patients (n=10)</th>
<th>Cardiac transplant patients (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>55±4</td>
<td>45±4</td>
</tr>
<tr>
<td>Coronary arteries</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>67±2</td>
<td>53±4</td>
</tr>
<tr>
<td>Months from transplant</td>
<td>...</td>
<td>17.3±3.4</td>
</tr>
<tr>
<td>Baseline values</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate (beats/min)</td>
<td>67±4</td>
<td>68±5</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>100±4</td>
<td>119±6</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

SN, sinus node.

over, it remained to be determined whether the bradycardia and hypotension result from stimulation of ventricular sensory endings, other cardiopulmonary endings, a direct nonneurogenic effect on the sinus node, or a combination of these factors.

The purpose of our study was to determine if the bradycardia and hypotension produced during coronary arteriography in humans occur as a result of stimulation of ventricular chemosensitive endings. We capitalized on the cardiac transplant model to test our hypothesis. Cardiac transplantation interrupts all innervation of the ventricles but leaves intact innervation (both afferent and efferent) of the recipient atria (including the sinus node) and lungs. Thus, if ventricular receptors serve as the afferent limb of the depressor reflex mentioned above, then their interruption would be expected to abolish the reflex. On the other hand, if reflex slowing of the innervated sinus node persisted after transplantation, then it could be suggested that receptors other than those in the ventricles contribute to the reflex responses to intracoronary contrast. The responses of the denervated donor heart were used to assess the possible direct (nonneural) effects of intracoronary contrast on the sinus node.

Methods

Subjects

Ten cardiac transplant patients and 10 control patients were studied during routine coronary arteriography for evaluation of possible coronary artery disease. Coronary arteries were normal in both groups as were left ventricular ejection fractions (Table 1). Four control patients were observed to have left-dominant circulations with small right coronary arteries. Neurologic or other diseases that impair neurologic function were absent in all patients. All cardiac transplant patients were receiving cyclosporine A and azathioprine or prednisone, or all three; six were receiving nifedipine; four, furosemide, or captopril, or both; two, β-blockers; and one, clonidine or labetalol. All control patients were receiving nitrates and five were receiving diltiazem and one each of either metoprolol, verapamil, lasix, clonidine, or theophylline. The study protocol was approved by the Human Subjects Review Committee of the Virginia Commonwealth University and McGuire Veterans Administration Medical Center, and written informed consent was obtained from all patients.

Measurements

Systemic arterial pressure was measured by a femoral artery catheter using saline-filled Hewlett-Packard pressure transducers. In the cardiac transplant patients, recipient sinus-node rate was determined by recording recipient right atrial electrogram (A-A interval) with a right atrial intracavitary electrode positioned posteriorly. Donor sinus-node rate (P-P interval) was determined from the surface electrocardiogram. In the control patients, P-P interval was recorded from surface electrocardiograms. A bellows-type respirometer was used to indicate inspiratory and expiratory movements. All signals were displayed on a Hewlett-Packard strip-chart recorder and, during coronary arteriography, were recorded at a paper speed of 100 mm/sec.

Protocol

All cardiac medications were withheld 12 hours before cardiac catheterization. Approximately 1 hour before the procedure, each patient was premedicated with diazepam 10 mg p.o. Each patient was instrumented, and then selective left (LCA) and right (RCA) coronary arteriography was performed with standard Judkins technique. A premeasured volume of meglumine diatrizoate (Hypaque-76, Winthrop Breon) was used for each injection (5-10 ml, dependent on arterial distribution). Measurements were recorded during each of two injections into each coronary artery. Recording was begun 10 beats before each injection and then continuously for 35 seconds after the start of injection to ensure recording of the maximum changes in P-P and A-A intervals and arterial pressure. Patients were instructed to breathe normally during each injection.

Data Analysis

All measurements were made at end expiration as indicated by the respirometer trace. For a given injection, baseline P-P and A-A intervals were measured as the average P-P and A-A intervals during the 10-beat control period and compared with the maximum P-P and A-A intervals after injection. Data are presented as change in heart rate in beats per minute calculated from the P-P interval for the donor, and control heart rate and A-A interval for recipient sinus-node rate. Mean arterial pressure was calculated by adding one third of the pulse pressure to the diastolic pressure, and baseline was
compared with the maximum change in mean arterial pressure after injection.

Statistical significance was determined using the paired or unpaired t test as appropriate. The Bonferroni procedure was used to correct for multiple comparisons. Values of p<0.05 were considered significant. Results are expressed in the tables, figures, and text as mean±1 SEM. Most of the variability represented by the SEM was due to differences between patients.

**Results**

Baseline values for control and cardiac transplant patients are illustrated in Table 1. Control heart rate and recipient sinus-node rate were nearly equal, whereas donor heart rate was elevated, reflecting the denervated state and lack of vagal tone. Mean arterial pressure in the transplant patients was elevated, probably secondary to immunosuppressant therapy with cyclosporine-A.

An original record obtained during coronary arteriography in a cardiac transplant patient is shown in Figure 1. Note that after injection (Figure 1B), the donor sinus-node rate (p-p interval on surface ECG) decreases, the recipient sinus-node rate (recipient atrial electrogram; A-A interval) increases, and femoral artery pressure decreases compared with baseline parameters recorded in Figure 1A.

The maximum change in mean arterial pressure in response to intracoronary contrast injection is illustrated in Figure 2 and Table 2. There was a significant decrease in mean arterial pressure in transplant patients (LCA, −12.7±2.3 mm Hg; RCA, −11.4±2.2 mm Hg) and controls (LCA, −18.7±1.7 mm Hg; RCA, −10.7±1.6 mm Hg). Responses were similar in both groups.

The maximum changes in donor heart rate and recipient sinus-node rate, in response to coronary contrast injection, are displayed in Figure 3 and Table 2. Despite the reduction in mean arterial

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** Analog tracings from patient with cardiac transplantation demonstrating measurement of donor sinus-node cycle length (surface electrocardiogram, P-P interval), recipient sinus-node cycle length (recipient atrial electrogram, A-A interval), and blood pressure (femoral artery pressure) recorded before (Panel A) and after (Panel B) contrast injection at time of maximum changes. CL, cycle length.

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Bar chart of maximum change in mean arterial pressure (MAP) in response to coronary arteriography in control and cardiac transplant patients. +, Significant change from baseline (p<0.0001); open and solid bars, left and right coronary injections.
pressure, there was a significant decrease in heart rate in the control patients during left (−15.3±2.3 beats/min) and right (−6.9±1.9 beats/min) coronary injections. In contrast, the recipient (innervated) sinus-node rate in the transplant patients increased significantly during left (6.6±1.7 beats/min) and minimally during right (2.4±1.4 beats/min) coronary injection. The responses of the recipient sinus node were not only significantly different from those observed in the control patients but were opposite in direction. The donor (denervated) sinus-node rate in the transplant patients decreased minimally during left coronary injection (−5.4±2.1 beats/min) and right coronary injection (−3.0±1.7 beats/min).

The donor sinus-node slowing occurred minimally, even though there was complete denervation of the donor heart. Therefore, this slowing was the result of a direct chemical-depressant effect of contrast on the donor sinus node. An increase in the recipient sinus rate (innervation intact) in the cardiac transplant patients was observed during contrast injection, in association with a decline in blood pressure. We postulated that this effect on the recipient sinus node was mediated mainly through arterial baroreceptor influences, resulting from the decline in blood pressure but which may have been modified by the direct influence of the ionic contrast agent. To provide an estimate of the isolated baroreceptor reflex influence on the recipient sinus node, we subtracted the donor (nonneural) heart-rate response from the recipient (neural plus nonneural) sinus-node rate response. These results are illustrated in Figure 4, in which RSNR−DHR represents this subtraction. A larger increase in recipient sinus-node rate is now evident (LCA, 12.0±3.5 beats/min; RCA, 5.4±2.2 beats/min), after the direct (nonneural) effects are removed. Following the same logic, we estimated the ventricular depressor-reflex influence on the control-patient sinus node by eliminating the direct effects and baroreceptor reflex effects of the recipient group. Thus, we subtracted the sinus-node response of the recipient group.

**TABLE 2. Maximum Changes in Mean Arterial Pressure and Heart Rate and Time to This Response After Coronary Contrast Injection**

<table>
<thead>
<tr>
<th></th>
<th>MAP (mm Hg)</th>
<th>Time 1 (sec)</th>
<th>HR (beats/min)</th>
<th>Time 2 (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Controls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCA</td>
<td>−18.7±1.7*</td>
<td>10.8±0.5</td>
<td>−15.3±2.3*</td>
<td>9.0±0.6†</td>
</tr>
<tr>
<td>RCA</td>
<td>−10.7±1.6*</td>
<td>11.8±0.6</td>
<td>−6.9±1.9*</td>
<td>9.8±1.5‡</td>
</tr>
<tr>
<td><strong>Cardiac transplant patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipient LCA</td>
<td>−12.7±2.3*</td>
<td>9.0±0.6</td>
<td>6.6±1.7*‡</td>
<td>10.5±0.8</td>
</tr>
<tr>
<td>Sinus node RCA</td>
<td>−11.4±2.2*</td>
<td>10.7±0.8</td>
<td>2.4±1.4‡</td>
<td>11.2±0.7</td>
</tr>
<tr>
<td>Donor LCA</td>
<td>−12.7±2.3*</td>
<td>9.0±0.6</td>
<td>−5.4±2.1‡</td>
<td>8.2±0.6</td>
</tr>
<tr>
<td>Sinus node RCA</td>
<td>−11.4±2.2*</td>
<td>10.7±0.8</td>
<td>−3.0±1.7</td>
<td>9.6±2.2</td>
</tr>
</tbody>
</table>

MAP, mean arterial pressure; time 1, time to maximum change in MAP; HR, heart rate; time 2, time to maximal change in HR; LCA, left coronary artery; RCA, right coronary artery.

*Significant changes from baseline (p<0.05); †Significant difference from time 1 (p<0.05); ‡Significant changes from control (p<0.05).

**Figure 3.** Bar chart of maximum change in sinus-node rate in response to coronary arteriography in control patients and cardiac transplant patients (recipient sinus node and donor sinus node). +, Significant change from baseline (p<0.05); *, significant difference between control and cardiac transplant patients (p<0.05).
(baroreceptor reflex plus direct contrast effect) from the sinus-node response of the control group (control sinus-node rate = baroreceptor reflex plus ventricular depressor reflex plus direct contrast effect). These results are also illustrated in Figure 4, in which control sinus-node rate minus recipient sinus-node rate (CSNR - RSNR) represents this subtraction. As expected, slowing is now more pronounced (LCA, -21.9 beats/min; RCA, -9.2 beats/min), once the effects produced by nonneural effects and by the baroreceptor reflex to decreasing blood pressure are removed. Table 3 summarizes the effect of coronary arteriography on the change in rates of the different sinus nodes examined in this study. The calculations used to isolate the different effects also are presented.

Table 2 illustrates the time to the maximum change in mean arterial pressure (time 1) and heart rate (time 2), after coronary-contrast injection for controls and transplant patients. For the controls, the time for maximal heart-rate slowing (time 2) occurred approximately 2.0 seconds before the maximal decrease in mean arterial pressure (time 1). For the cardiac transplant patients, the time for maximal increase in recipient sinus-node rate tended to follow the maximal change in the mean arterial pressure for left and right coronary arteries, respectively. This is in keeping with our postulate that the increase in recipient sinus-node rate was a baro reflex-mediated response to the fall in arterial blood pressure. Maximal slowing of the donor sinus node (nonneural effect) occurred before the maximal change in blood pressure.

Discussion

Previous studies in humans have suggested that bradycardia during coronary arteriography is mediated, in part, by the cardiac-depressor (Bezold-Jarisch) reflex. For sinus slowing to occur, chemosensitive endings in the heart subserved by vagal afferents and vagal efferents to the heart must be intact. Eckberg et al. and White et al. investigated this reflex through chemical blockade of the efferent limb with atropine. They concluded that contrast-induced bradycardia was mediated mainly through reflex activation of vagal efferent nerves to the sinus node, but they were unable to provide information regarding the origin of the afferent limb of this reflex. Studies in animals have shown that certain chemicals, among them radiographic contrast, can activate ventricular sensory endings and also produce bradycardia and hypotension. We postulated that reflex responses during coronary arteriography in humans are due specifically to stimulation of ventricular chemosensitive endings. This hypothesis has not been tested previously. Our study is unique because we examined the response to coronary arteriography in a model of mainly ventricular deafferentation, enabling us to determine if ventricular sensory endings serve as the origin of the sensory input that results in reflex cardiac slowing.

During cardiac transplantation, the recipient ventricles and portions of the atria are removed, leaving only remnants of the atria. The great vein–atrial junctions and recipient sinus node remain in situ. Most of the vagal sensory endings in the atria are clustered around the venoatrial junctions. Recent work from our laboratory has indicated that efferent innervation to the recipient sinus node remains intact. Cardiac transplantation is completed by suturing the donor ventricles and portions of the atria to the recipient atrial remnants. Thus, the donor ventricles and donor sinus node are denervated, whereas the recipient sinus node and great vein–atrial junctions remain innervated (both efferent and afferent). If the afferent limb of the depressor reflex resides solely in the ventricles, then the afferent limb of the reflex would be interrupted by cardiac transplantation, but the efferent limb to the recipient sinus node would remain intact. Given the above condition, we hypothesized that contrast-induced bradycardia of the recipient sinus node would be abolished during coronary arteriography in cardiac transplant patients. Similarly, any slowing of the denervated donor sinus node would be due to a direct effect of contrast media on the sinus tissue.

Coronary arteriography in the control subjects produced the expected heart-rate slowing and blood-pressure decline. In contrast, the recipient sinus node accelerated in the cardiac transplant patients.
due to arterial baroreflex mechanisms in the absence of the cardioinhibitory influences of the ventricular receptors. The latter effect resulted from interruption of afferent fibers that subserve ventricular chemosensitive endings.

It is known that there are both chemosensitive and mechanosensitive endings subserved by vagal afferents in the myocardium. We considered the possibility that interruption of afferent fibers to ventricular mechanosensitive endings may have contributed to the absence of slowing of the recipient sinus node. Ventricular C-fiber activity from mechanosensitive endings has been shown to increase mainly in response to increases in diastolic pressure and by increasing the inotropic state of the ventricle. Intracoronary injection of meglumine diatrizoate, however, does not raise left ventricular end-diastolic pressure and is known to depress myocardial contractility, and this factor, coupled with a fall in systolic pressure, would tend to reduce the firing of mechanosensitive endings, making it unlikely that they contribute significantly to the reflex bradycardia that occurs with coronary arteriography in innervated control subjects.

It is also possible that atrial sensory endings may be activated by meglumine diatrizoate and participate in contrast-induced reflex slowing in normal subjects. As stated above, because efferent innervation to the recipient atria remains intact, it is likely that afferent innervation to this area is intact, as well. If recipient atrial sensory endings mediate the reflex response, then their stimulation would be expected to slow the recipient sinus node. Because it did not slow, either these endings did not contribute significantly or they were not stimulated sufficiently. The latter would depend on the blood supply to the recipient atrium, which may be altered after cardiac transplantation. Our experimental model did not allow us to determine if atrial endings were adequately stimulated. Studies by Dawes and Comroe in animals, however, suggest that left ventricular sensory endings are mainly responsible for the depressor reflexes produced with injection of veratridine into the cardiopulmonary region. Collectively, the aforementioned data suggest that bradycardia produced during coronary arteriography in innervated hearts is mediated, in large part, through a depressor reflex activated by stimulation of ventricular chemosensitive endings.

An increase in the recipient sinus-node rate was observed during contrast injection in the cardiac transplant patients. Because, as previously noted, there was a decline in blood pressure with contrast injection, it is likely that this increase in rate was mediated through activation of arterial baroreflexes. This effect was only apparent after the cardiac-depressor reflex was eliminated in the transplant patients. These data suggest that the combined effects of the cardiac-depressor reflex and direct sinus-node depression usually override those of the arterial baroreflex during coronary arteriography in innervated hearts. It follows that, in innervated hearts, the arterial baroreflex may act as a buffer against excessive bradycardia that might otherwise occur during coronary arteriography. It is also of interest that, after contrast injection in the control patients, the time to the maximum change in heart rate occurred before the maximal change in mean arterial pressure (Table 2). This can be explained by the fact that the slowing of the control-patient sinus node was due to a primary ventricular depressor-reflex response from contrast. In contradistinction, the speeding of the recipient sinus node in the transplant patients was due to a baroreflex response that first required a drop in blood pressure.

In patients with cardiac transplantation, the recipient sinus node remains innervated, but the transplanted donor atria (including the sinus node) and ventricles are devoid of both afferent and efferent innervation. Modest slowing of the denervated donor sinus node was observed during coronary arteriography. Because this slowing occurred when both the afferent and efferent limbs of the depressor reflex were completely eliminated, it must have been mediated through a direct effect of contrast on the donor sinus node, as previously discussed. These results are similar to those of Eckberg et al and White et al, who also observed an attenuation in cardiac slowing during coronary arteriography, after efferent limb blockade with 2.0–3.6 mg atropine i.v. Thus, meglumine diatrizoate can produce a direct depressant effect on the sinus node in humans. If we eliminate the direct effect of contrast by subtracting the donor heart-rate response from the recipient sinus-node rate response, the independent baroreflex effects of contrast medium then are evident (Figure 4).

We can also characterize the independent contribution of the ventricular chemoreceptor reflex by subtracting the recipient sinus-node rate response (no ventricular receptors plus intact arterial baroreflex plus direct effect of contrast) from the control-patient sinus-node rate response (intact ventricular chemoreflex plus intact arterial baroreflex plus direct effect of contrast). As illustrated in Figure 4, for control sinus-node rate minus recipient sinus-node rate, the “independent” contribution of ventricular sensory endings to contrast-induced slowing of heart rate, is quite significant. We assumed that the sensitivities of the three sinus nodes (control, recipient, and donor) to the contrast agent were similar and that the baroreflex sensitivity of recipient and control sinus nodes was also similar. This has been shown previously to be the case. We also assumed that the responses of the control and recipient sinus nodes to the influences of contrast and the reflexes were linear and, therefore, additive.

Perez-Gomez and Garcia-Aguada observed that bradycardia was greatest when angiographic contrast was injected into the artery supplying the
inferior wall of the left ventricle. They also interpreted their findings to suggest that contrast-induced bradycardia may be reflexively mediated through stimulation of ventricular sensory endings. Previously, work in dogs also has suggested that ventricular sensory endings with vagal afferents are preferentially distributed to the inferoposterior left ventricular wall. With injection into the right coronary artery in our control patients there was less slowing produced than expected. Although it is not possible to be certain of the basis for this difference between our findings and those reported previously, we offer two explanations. First, four of the 10 control patients studied had left-dominant coronary circulations and the inferior wall was, thus, perfused from the left system. This would be expected to give rise to larger reflex responses to left coronary injection in innervated hearts. Eckberg and colleagues also failed to demonstrate a dominant response to right coronary injection. They did not report the incidence of left coronary dominance in their patients. In addition, amounts of contrast required to opacify the left are larger than required by the right coronary artery, possibly resulting in greater activation of ventricular sensory endings in the anterior wall of the left ventricle.

Other factors may have accounted for differences in the responses to left and right coronary injection of the recipient sinus node in cardiac transplant patients. The blood supply to the recipient sinus node does not originate from the coronary circulation of the transplanted heart in the normal manner, and may traverse areas of neovascularization across suture lines between the remnant and donor right atrium or from collaterals from arteries perfusing the superior vena cava. More direct perfusion of the recipient sinus node may have occurred with right coronary injection, and therefore, a direct depressant effect may have opposed the positive chronotropic influence of the arterial baroreflex. As illustrated in Figure 3, there was less cardioacceleration with right than with left coronary injection. This difference may be attributable to greater direct (nonneural) effects of contrast during right coronary injections, especially because the reflex effects due to a similar decrease in blood pressure should have been the same (Figure 2).

The changes in mean arterial blood pressure during right and left coronary-contrast injection were similar in both groups of patients, suggesting that these responses in the transplant patients were not reflex mediated. Eckberg et al and White et al observed that the administration of atropine significantly reduced the hypotension observed with coronary-contrast injection. Part of this effect may have been due to the abolition of the decreased cardiac output that would be expected to accompany bradycardia, although this issue remains unresolved. The blood pressure reduction observed in the cardiac transplant patients may have occurred from the negative inotropic effect of contrast in a heart without sympathetic support.

We have used the cardiac transplant model that results in mainly ventricular deafferentation to examine the roles of ventricular sensory endings in the bradycardia and hypotension that occurs during coronary arteriography. Our observations suggest that contrast-induced bradycardia is mediated predominantly through the cardiac-depressor reflex, which originates from chemosensitive endings in the ventricles. Contrast medium also was observed to produce a direct depressant effect on the sinus node, resulting in mild sinus slowing. Our data also suggest that the cardiac-depressor reflex strongly influences the cardiovascular system during coronary arteriography and overrides the effects of the arterial baroreflexes. The net responses in subjects with intact innervation are the results of the integration of ventricular reflexes, arterial baroreflexes, and direct effects of contrast on the sinus node.

Acknowledgments

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