Effect of Chronic Myocardial Infarction on Vagal Cardiopulmonary Baroreflex

Anthony J. Minisi and Marc D. Thames

Sensory endings in the left ventricle are damaged by acute myocardial infarction. The goal of our experiments was to determine whether reflexes that originate in the heart are impaired by chronic myocardial infarction. Inferoposterior (n=11) or anterior (n=10) infarction was produced in dogs by ligation and intracoronary injection of rapidly hardening latex into either the proximal left anterior descending or left circumflex coronary arteries. Four weeks after infarction, the changes in renal sympathetic nerve activity induced by phenylephrine infusion, hemorrhage, and volume expansion were assessed before and after sinoaortic baroreceptor denervation. The results in infarct dogs were compared with the results in 11 sham-operated dogs. With arterial baroreceptors intact, baroreflex sensitivity (defined as the percent change in renal nerve activity per millimeter of mercury change in mean pulmonary artery wedge pressure) was similar in all groups of dogs. Following sinoaortic denervation, dogs with anterior and inferoposterior infarction had impaired responses to volume expansion. The responses during hemorrhage were abolished in dogs with inferoposterior infarction. We conclude that chronic myocardial infarction impairs reflexes that originate in the heart in response to changes in cardiac filling pressures. (Circulation Research 1989;65:396-405)

Sensory receptors with vagal afferents are located throughout the cardiopulmonary region. Many of these receptors respond to changes in blood volume and cardiac filling pressures. Activation of sensory endings with vagal afferents produces reflex cardioinhibitory and vasodepressor responses as well as inhibition of efferent sympathetic nerve activity. Despite the ubiquity of these receptors in the cardiopulmonary region, recent evidence from patients with heart transplantation suggests that cardiac receptors, especially those in the ventricles, are particularly important in mediating these responses. Moreover, experiments in which ventricular receptors were stimulated by myocardial ischemia indicate that the ventricular receptors are preferentially distributed to the inferoposterior wall of the left ventricle. Barber et al have shown that acute myocardial infarction interrupts vagal afferents and abolishes reflex vasodepressor responses induced by chemical activation of these sensory endings. There are no data on the effects of chronic myocardial infarction on reflexes originating from the cardiopulmonary region in response to mechanical activation of sensory endings. Our experiments were designed to determine the effect of chronic inferoposterior and anterior myocardial infarction on reflexes activated by a physiological stimulus and mediated by cardiac receptors with vagal afferents. We hypothesized that destruction of ventricular sensory endings by chronic infarction would produce abnormalities in reflex responses to changes in cardiac filling pressures.

Materials and Methods

Mongrel dogs of both sexes weighing 18-30 kg were anesthetized with thiopental sodium (25 mg/kg i.v.) in preparation for left thoracotomy under aseptic conditions. Once a surgical plane of anesthesia was obtained, the animals were intubated and ventilated. Supplemental doses of thiopental (25-125 mg i.v.) were given at intervals to maintain a surgical plane of anesthesia. Following suspension of the heart in a pericardial cradle, the proximal segment of either the left anterior descending or left circumflex coronary artery was isolated. In the sham (SHM) group of dogs, the pericardium and chest then were closed, and the animals were allowed to recover. In the remaining dogs, the isolated coronary artery (left anterior descending or circumflex) was ligated and injected with a rapidly hardening
latex suspension. This method has been shown to consistently produce a well-demarcated, transmural myocardial infarction. Postoperatively, the animals were treated with penicillin G (600,000 units i.m. b.i.d. for 7 days). Meperidine (11 mg/kg i.m. every 3 hours) was administered as needed for postoperative pain.

After a recovery period of approximately 28 days (range, 16–75 days), the animals again were anesthetized with thiamylal sodium (15 mg/kg i.v.) followed by α-chloralose (80 mg/kg i.v.). After endotracheal intubation, the animals were placed on a ventilator and were ventilated with a mixture of oxygen and room air. Arterial blood gases were determined at intervals, and either the respiratory settings were adjusted or sodium bicarbonate was administered to maintain the pH between 7.35 and 7.45. Additional doses of α-chloralose (10 mg/kg) were administered hourly. Arterial and venous cannulae were placed in the femoral vessels and a Swan-Ganz catheter was passed into the pulmonary artery via the external jugular vein. The surface electrocardiogram, arterial pressure, and mean pulmonary artery pressure were monitored continuously during the protocol.

An incision then was made in the left flank to expose the left renal artery. A small branch of the renal sympathetic nerves was identified and dissected free from the renal artery and the adjacent connective tissue. The nerve was sectioned, and the nerve sheath was removed. The nerve was immersed in mineral oil and placed on bipolar platinum electrodes for recording of action potentials as previously described in detail. In brief, the signal was amplified by a band-pass amplifier (model P511, Grass Instruments, Quincy, Massachusetts) with high frequency cutoff set at 1,000–3,000 Hz and low frequency cutoff set at 30–100 Hz. The output of this amplifier was fed into a spike counter that counted and integrated all nerve spike activity whose amplitude exceeded a preselected voltage level (just above noise). During nerve recordings, pancuronium bromide (2 mg i.v.) was administered to prevent movement. Each dose of pancuronium was allowed to wear off before additional doses were given to permit determination of the adequacy of anesthesia.

We determined the changes in mean arterial pressure, mean pulmonary artery pressure and pulmonary artery wedge (PAW) pressures, and integrated efferent renal sympathetic nerve activity (RSNA) during elevation of arterial pressure by infusion of phenylephrine (PE) and during changes in cardiac filling pressures induced by hemorrhage and volume expansion. PE was infused at 17–256 μg/min to achieve a gradual elevation of arterial pressure over 4–7 minutes. Hemorrhage was performed in three stages by removal of 5 ml/kg over 2½ minutes during each stage for a total of 15 ml/kg removed. Volume expansion was performed in a similar fashion using either 10% dextran or 6% hetastarch in normal saline. In all cases, the shed blood was rein infused, or the infused volume was removed. Adequate time for stabilization of hemodynamic parameters was interpolated between interventions. These maneuvers were performed before and after denervation of the aortic and carotid baroreceptors.

To denervate the arterial baroreceptors, a midline cervical incision was made, and the carotid arteries were exposed bilaterally. The carotid baroreceptors were denervated by ligating and sectioning all of the structures that course between the internal and external carotid arteries. The adequacy of denervation was assessed by the failure of bilateral carotid occlusion and release to elicit changes in heart rate, blood pressure, or RSNA. The aortic baroreceptors were denervated by sectioning the cervical aortic nerves bilaterally. These nerves were dissected free in the vagosympathetic trunks just caudal to the nodose ganglia near the junctions of the vagi and the superior laryngeal nerves. The aortic nerves were identified by recording typical pulse synchronous baroreceptor afferent activity. The adequacy of aortic arch denervation was determined by analysis of renal nerve activity changes during PE-induced elevation of arterial pressure after sinoaortic denervation (SAD).

At the completion of the protocol, the dogs were killed, and their hearts were removed. Transverse sections of 0.5–1.0 cm thickness were made in the left ventricle and interventricular septum from apex to base. The sections were incubated for 30 minutes in a 1% solution of tetrazolium red at 35°C. After staining, the infarcted myocardium was carefully separated from the noninfarcted myocardium. The extent of infarction was expressed as the ratio of the weight of the infarcted segments to the weight of the entire left ventricle.

Data Analysis

Measurements of mean arterial pressure, mean pulmonary artery pressure, PAW pressure, and integrated renal nerve activity were made at baseline before each intervention, during several levels of arterial pressure elevation with PE infusion, and after each stage of either hemorrhage or volume expansion. The measurements made during each maneuver were compared with the basal values. Responses of nerve activity were expressed as percent change from baseline rather than in absolute values because the absolute value of nerve activity is dependent on the number of fibers placed on the recording electrodes, and the number of fibers varies from one preparation to another. The values for all dogs in each of the three groups (SHM, left anterior descending infarct [LAD], and left circumflex infarct [LCx]) were combined, and mean±SEM were calculated. These mean values were used in subsequent statistical analysis. Multivariate analysis of variance was employed to determine the significance of the differences among the groups in the changes of the measured parameters.
FIGURE 1. Changes in mean arterial pressure (MAP), mean pulmonary artery pressure (PA), and percent change in efferent renal sympathetic nerve activity (RSNA) during phenylephrine (PE) infusion are illustrated for all groups of dogs before (left panel) and after (right panel) sinoaortic denervation (SAD). Measurements were made in each dog at baseline (B) and at random intervals (T1, T2, T3) as the arterial pressure rose during PE infusion. All values are mean±SEM. There are no significant differences between the groups in the changes of any of these parameters. LCx, left circumflex infarct group; LAD, left anterior descending infarct group; SHM, sham group.

that occurred during each maneuver. Analysis of covariance was used to determine if there were significant differences among the groups in the slopes of the regression lines relating changes in renal nerve activity to changes in arterial or PAW pressures. Unpaired *t* tests were used to determine the significance of differences between the groups in infarct size and in PAW pressure at baseline. A Bonferroni correction was used when multiple paired comparisons were made. A value of *p*<0.05 was considered to be statistically significant.

Results

Experiments were completed in 11 dogs each in both the SHM and LCx groups. There were 10 dogs in the LAD group. One SHM dog and two LAD dogs did not have adequate SAD. Therefore, only the pre-SAD results were analyzed in these dogs. None of the dogs in any of the groups had clinical evidence of congestive heart failure postoperatively or at the time of final study. There were no significant differences in the PAW pressures measured at the start of the protocol (SHM, 6.4±0.9 mm Hg; LCx, 7.5±1.0 mm Hg; LAD, 6.1±1.5 mm Hg). The infarct size was significantly larger in the LCx group than in the LAD group (25.6±1.8% vs. 15.7±2.4%; *p*<0.05) although there was extensive overlap in the range of sizes in the two groups (LAD, 5–32%; LCx, 13–33%). All infarcts were transmural and well-demarcated.

Responses to Phenylephrine Infusion

The changes in hemodynamic parameters and nerve activity that occurred during PE infusion in each group are summarized in Figure 1. With the sinoaortic baroreflexes intact, elevation of systemic arterial pressure by PE resulted in similar inhibition of RSNA in each group. The presence of anterior or inferoposterior infarction had no appreciable effect on the modulation of sympathetic outflow by the arterial baroreceptors in response to increases in blood pressure. After SAD, the changes in RSNA associated with blood pressure elevation were greatly diminished, indicating adequate denervation of the arterial baroreceptors. Modest sympathoinhibition persisted during PE infusion in the post-SAD dogs. This correlated better with elevation of pulmonary artery pressures than with elevation of arterial...
Increases in arterial pressure in the absence of increases in pulmonary artery pressure failed to change renal nerve activity. Thus, the changes observed after SAD likely were mediated by cardiopulmonary receptors rather than by residual arterial baroreceptors. This effect of pulmonary arterial pressure changes during PE infusion is the subject of a separate report.15

Figure 2 illustrates the relations between changes in arterial pressure and changes in nerve activity during PE infusion. Analysis of the data in this fashion is important since the slopes of these relations (percent change in RSNA per millimeter of mercury change in mean arterial pressure) provide an estimate of the sensitivity of arterial baroreflex control of RSNA. Before SAD, there were no significant differences among the groups in baroreflex sensitivities (LCx, -2.67±0.12; LAD, -2.93±0.51; SHM, -2.56±0.16; p=NS). After denervation of the arterial baroreceptors, the expected decrease in arterial baroreflex sensitivity was observed, but there were no significant differences noted among the three groups (LCx, -0.90±0.24; LAD, -0.62±0.10; SHM, -0.84±0.08; p=NS).

Responses to Hemorrhage

The changes in mean arterial pressure, PAW pressure, and RSNA that occurred in each group of dogs during hemorrhage are illustrated in Figure 3. With the arterial baroreceptors intact, appropriate increases in RSNA were noted in each group. Hemorrhage was not a selective stimulus for the cardiopulmonary receptors. Significant decreases in arterial pressure occurred during hemorrhage in each group. Thus, changes in RSNA during this maneuver were mediated by both arterial and cardiopulmonary baroreceptors. In the LAD dogs, the changes in nerve activity and PAW pressure tended to be greater than in the other two groups, but this difference did not reach statistical significance. The changes in arterial pressure were similar in all three groups. It is likely that the greater degree of sympathoexcitation in the LAD group was related to the larger fall in PAW pressure. This larger fall in pressure would have a more powerful effect on the activity of the afferent endings and would result in a greater reflex response.

After SAD and elimination of nerve traffic changes mediated by arterial baroreflexes, there were significant increases in RSNA in response to hemorrhage-induced decreases in cardiac filling pressures in the LAD and SHM dogs. However, the sympathoexcitatory response was abolished in the dogs with inferoposterior infarction (p<.05 LCx vs. LAD and SHM). This difference was probably not due to any disparity in the stimulus to the cardiopulmonary receptors. Although the absolute values of PAW pressure were lower in the LAD group compared with the LCx and SHM groups, the changes in pressure that were elicited by hemorrhage were not different among the three groups (LCx, -4.4±1.0; LAD, -4.7±1.0; SHM, -3.4±0.8; p=NS).

Figure 4 illustrates the relations between the changes in RSNA and the changes in PAW pressure that occurred during hemorrhage. As with the PE data above, this analysis is important because the slopes of these relations (percent change RSNA per millimeter of mercury change PAW pressure) provide an estimate of the sensitivity of cardiopulmonary baroreflex control of renal nerve activity. With the sinoaortic baroreceptors intact, there were no significant differences in reflex sensitivity among the three groups (LCx, -19.60±1.99; LAD, -30.43±5.65; SHM, -22.69±1.70; p=NS). Post-SAD, the markedly abnormal responses of the LCx group (-59±2.51) compared with the LAD (-21.32±7.34) and the SHM (-20.76±0.85) groups are obvious. The differences between the responses before and after SAD provide an estimate of the contribution of arterial baroreflexes to the integrated responses observed before SAD.

Responses to Volume Expansion

The responses of hemodynamic variables and RSNA to volume expansion are illustrated in Figure 5. All groups demonstrated a comparable and appropriate decline in RSNA with elevations of cardiac filling pressures. Unlike hemorrhage, volume expansion had negligible effects on arterial pressure when the arterial baroreceptors were intact. Thus, this stimulus can be considered as relatively selective
for vagal cardiopulmonary receptors. To further support this contention, the responses of heart period (msec) during volume expansion in each group are listed in Table 1. The lack of consistent heart period slowing with volume infusion indicates that the arterial baroreceptors were not stimulated and probably contributed little to the responses of efferent nerve traffic.

After SAD, volume expansion continued to result in sympathoinhibition, the overall magnitude of which seemed unaffected by the presence of an anterior or inferoposterior infarction. However, when the relations between the changes in RSNA and the changes in PAW pressures are examined after SAD (Figure 6), there were blunted responses in both the LAD (-4.68±0.49) and LCx (-5.57±0.71) dogs compared with SHM (-11.20±0.49; p<0.05 LAD and LCx vs. SHM). This indicates reduced baroreflex sensitivity for increases in filling pressures after both anterior and inferoposterior infarction. Before SAD, there were no significant differences among the groups.

Discussion

Cardiac receptors with vagal afferents exert a tonic inhibitory influence on sympathetic outflow from the vasomotor centers. Stimulation of these receptors has been shown to result in reflex bradycardia and vasodilation. This depressor response is related both to withdrawal of sympathetic outflow to the heart and peripheral circulation and to augmentation of efferent vagal activity to the heart. Acute myocardial ischemia and infarction activate cardiac receptors with vagal afferents, especially those in the left ventricle. This activation is related to systolic bulging of the ischemic myocardium and possibly to release of substances such as potassium, bradykinin, and prostaglandins during ischemia. Although stimulation of cardiac receptors by myocardial ischemia produces reflex depressor responses in dogs, the effects of chronic myocardial infarction and myocardial fibrosis on the function of cardiopulmonary reflexes have not been studied extensively. Barber et al have shown that acute transmural myocardial infarction results in destruction or malfunction of cardiac afferent and efferent fibers traversing the infarcted zone. Barber and colleagues examined the reflex responses to chemical stimulation of sensory endings within hours of infarction. The purpose of our
study was to determine if chronic myocardial infarction alters reflex responses to mechanical stimulation of receptors in the cardiopulmonary region. We examined the reflex responses mediated by cardiac mechanoreceptors with vagal afferents in response to changes in cardiac filling pressures. We also sought to investigate whether disruption of afferent input from cardiac receptors would perturb the reflexes mediated by the arterial baroreceptors in response to elevations of systemic arterial pressure.

Our results indicate that reflexes that originate in the heart are impaired by myocardial infarction. Specifically, the presence of inferoposterior infarction greatly attenuated the increases in efferent RSNA that occur with decreases in cardiac filling pressures induced by hemorrhage. This abnormality was most apparent when the influence of the arterial baroreceptors was removed by SAD. A significant fall in arterial pressure occurred during hemorrhage. This fall in pressure likely resulted in recruitment of sinoaortic baroreflexes when the arterial baroreceptors were intact. The reflex sympathoexcitation associated with this recruitment may have obscured the detection of an abnormal response to hemorrhage in dogs with inferoposterior infarction and intact arterial baroreceptors.

It is surprising that the reflex sensitivity to hemorrhage was not modified by SAD in the SHM group, since a fall in arterial pressure also occurred with pre-SAD hemorrhage in this group. This observation may provide further insight into the relative roles of the vagal cardiopulmonary and arterial baroreflexes in the control of renal nerve activity during volume changes. A previous study by Thames et al. demonstrated that denervation of the sinoaortic baroreceptors had no major effect on the inhibition of renal nerve traffic during volume expansion. They concluded that reflex control of renal nerve activity during volume expansion was mediated predominantly by the vagal cardiopulmonary baroreflex. The results of our study indicate that the same conclusion may be applicable to the control of renal nerve activity during hemorrhage.

The impairment of circulatory reflexes that we observed following inferoposterior myocardial infarction is consistent with the results of other studies. Experimental evidence in dogs and clinical observations in humans indicate that cardiac receptors with vagal afferents are preferentially distributed to the inferoposterior wall of the left ventricle. Thus, destruction of sensory endings following inferoposterior infarction would be most likely to impair reflex responses normally mediated by cardiac receptors.

In contrast to the dogs with inferoposterior infarction, the dogs with anterior infarction continued to respond to decreases in cardiac filling pressures in an appropriate manner even after arterial baroreceptor denervation. Before SAD, the LAD infarct group actually showed an exaggerated nerve activity response when compared with the SHM group. However, this response was most likely related to a greater fall in PAW pressure in this group during hemorrhage. When the sensitivities of the reflex responses were evaluated, there were no significant differences between the groups.

Unlike the results noted during hemorrhage, the presence of anterior or inferoposterior infarction had only a modest effect on sympathoinhibitory responses during volume expansion. After denervation of the arterial baroreceptors, the slope of the relation between changes in nerve activity and changes in PAW pressure was blunted in both groups of infarct dogs compared with SHM. Thus, although dogs with infarction were capable of responding to increases in cardiac filling pressure, the sensitivity or gain of the reflex response was altered by infarction. Neither group of infarct dogs had noticeable impairment of arterial baroreflex-
mediated inhibition of sympathetic outflow in response to arterial pressure elevation by phenylephrine infusion.

The most likely explanation for our observations is that infarction results in the destruction of cardiac receptors located preferentially in the inferoposterior left ventricle. This destruction eliminates afferent input from this group of receptors and alters the reflexes mediated by them. The greatest abnormalities were evident during decreases in cardiac filling pressures. While the ventricular receptors have been shown to be preferentially distributed to the inferoposterior wall, there are vagal sensory receptors throughout the cardiopulmonary region. Our results indicate that the ventricular receptors are particularly important in the reflex responses to decreases in cardiac filling pressures. Other receptors in the cardiopulmonary region may continue to mediate a response to increases in filling pressures when ventricular receptors are damaged, although abnormalities in the gain or sensitivity of this response become apparent when the sinoaortic baroreceptors are denervated. Similar evidence is emerging from another model of ventricular deafferentation—human cardiac transplantation. Studies on these patients indicate that responses are markedly abnormal during maneuvers, such as lower body negative pressure, that unload cardiopulmonary receptors. The transplant model is similar to our canine model in that ventricular receptors are

Table 1. Values of Heart Period (msec) Observed in All Groups of Dogs During Volume Expansion With Intact Arterial Baroreceptors

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>Vol 5</th>
<th>Vol 10</th>
<th>Vol 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCx</td>
<td>471 ± 39.5</td>
<td>472 ± 42.9</td>
<td>460 ± 33.0</td>
<td>450 ± 27.7</td>
</tr>
<tr>
<td>LAD</td>
<td>476 ± 29.7</td>
<td>483 ± 28.2</td>
<td>462 ± 26.7</td>
<td>483 ± 34.6</td>
</tr>
<tr>
<td>SHM</td>
<td>424 ± 38.0</td>
<td>433 ± 38.0</td>
<td>424 ± 30.6</td>
<td>410 ± 30.0</td>
</tr>
</tbody>
</table>

All values are mean ± SEM. Measurements were made at baseline and at the end of each stage of volume infusion. The changes that occurred during the intervention are not significantly different from the baseline values in any of the groups. LCx, left circumflex infarct group; LAD, left anterior descending infarct group; SHM, sham group; Vol 5, volume expansion at 5 ml/kg 10% dextran or 6% hetastarch; Vol 10, volume expansion at 10 ml/kg 10% dextran or 6% hetastarch; Vol 15, volume expansion at 15 ml/kg 10% dextran or 6% hetastarch.
denervated but vagal sensory endings in the atria, great veins, and remainder of the cardiopulmonary tree are thought to remain undisturbed. Is there other physiological evidence that vagal ventricular receptors could play a role in reflex adaptations to hemorrhage and decreases in cardiac filling pressures? First, Mancia and Donald have demonstrated that vagal afferents in the ventricles exert tonic inhibition of the vasomotor center in dogs. Using a preparation in which the ventricles could be isolated (atria and lungs removed), they showed that interruption of afferent input from the ventricles by vagal cold block resulted in increases in sympathetic outflow. This interruption of afferent input by vagal cooling mimics the deactivation of cardiopulmonary receptors by decreases in cardiac filling pressures during hemorrhage. Second, the studies in human transplant patients alluded to above support our view that ventricular receptors play the dominant role in this reflex adaptation to decreases in cardiac filling pressures. Finally, Oberg and Thoren have provided direct neurographic evidence that ventricular receptors with vagal C fiber afferents, which have a low discharge frequency in the basal state, decrease their discharge frequency further during moderate degrees of hemorrhage. Thus, we feel that there is compelling evidence from reflex studies and from recordings from ventricular afferents to suggest that ventricular receptors are important in reflex adjustments to decreases as well as increases in cardiac filling pressures.

In our study, markedly abnormal responses to hemorrhage were observed following interruption of afferent input from the region in which vagal ventricular receptors are known to be preferentially distributed. Therefore, these results can be interpreted to add further support for the importance of ventricular receptors during receptor unloading.

The effects of infarction on regional or global systolic and diastolic ventricular function were not determined in our experiments. It is possible that the impaired reflexes we observed could be related to alteration of ventricular performance parameters such as compliance. In regard to responses limited to the LCx group could be explained by the larger infarct size in this group. Although ventricular compliance is difficult to quantify, it is reasonable to assume that infarction will either have no effect or will decrease compliance. Intravascular infusion and removal of similar volumes resulted in similar changes in cardiac filling pressures in each group of dogs. Figure 7 illustrates the changes in PAW pressure that occurred during hemorrhage and volume expansion in all groups of dogs after SAD. The relations obtained from the pre-SAD dogs were very similar to those illustrated in Figure 7. Note that the animals with anterior infarction appear to have the steepest pressure-volume relation, although this difference did not achieve statistical significance. This suggests that overall compliance of the capacitance vessels (which includes the cardiopulmonary region) was approximately equal. We acknowledge that this is not a direct measure of ventricular compliance. Thus, we cannot exclude the possibility that myocardial infarction alters ventricular compliance and the receptor stimulus-response relation in a manner that would produce the results we have observed. Although the
infarct size was significantly larger in the LCx group, there was considerable overlap between the LCx and LAD groups. Abnormal responses were apparent in dogs with both small and large inferoposterior infarctions. In addition, none of the dogs manifested clinical evidence of congestive heart failure, and there were no significant differences in baseline PAW pressures among the groups. Nevertheless, it could be suggested that the larger infarct size in the LCx group compromised ventricular activity to an extent that sympathetic nerve activity was at near maximal levels after SAD. Such a situation would provide an alternative explanation for the failure of renal nerve activity to increase further during hemorrhage. Although this possibility cannot be excluded definitively, we feel that it is unlikely for several reasons. First, there were no significant differences between the groups in the absolute baseline values (impulses per second) of nerve activity observed after SAD before hemorrhage (LCx, 99.8±22.3; LAD, 77.6±9.9; SHM, 110.4±24.2; p=NS). We acknowledge that analysis of the nerve traffic data in this manner must be interpreted with caution since we recorded from multunit preparations. Second, there was no correlation between infarct size and prehemorrhage baseline nerve traffic in the post-SAD animals with inferoposterior infarction (i.e., traffic was not related directly to infarct size). Finally, an impaired response to post-SAD hemorrhage in dogs with inferoposterior infarcts was clearly evident in animals with low baseline nerve activity. All of the above factors suggest that the abnormal reflexes we observed were related to the location of the infarct and the effect of infarction on afferent pathways rather than infarct size or infarct-related alteration of ventricular function.

Could the results of our study have been affected by the use of anesthetics? There is little dispute that the evaluation of the physiological role of circulatory reflexes is most accurately assessed in the conscious state. However, results from other studies indicate that α-chloralose anesthesia does not markedly alter reflex renal nerve responses during maneuvers such as PE infusion, hemorrhage, and volume expansion. The renal nerve activity changes we observed during PE infusion and volume changes were directionally similar to those described by Morita and Valter and during similar maneuvers in conscious dogs. Goel et al. noted that heart rate responses to hemorrhage were similar in conscious and α-chloralose-anesthetized animals. Thames and Kontos made similar observations concerning the heart rate responses to administration of vasodepressant drugs. We acknowledge that α-chloralose may alter the sensitivity of arterial and cardiopulmonary reflex control of renal nerve activity, although we are not aware of any data that support this view. However, there is no reason to expect that such an effect would be more pronounced in any one of our experimental groups.

Therefore, we do not feel that the use of anesthesia negates the major findings of this study.

In conclusion, our data indicate that chronic myocardial infarction impairs reflexes that originate in the heart. This impairment consists of an abnormal response to increases in cardiac filling pressures in dogs with both anterior and inferoposterior infarction and abolition of the response to decreases in cardiac filling pressure in dogs with inferoposterior infarction. The impaired responses are apparent only after denervation of the sinoaortic baroreceptors. Arterial baroreflex control of renal nerve activity is preserved after myocardial infarction. When the arterial baroreceptors are intact, the responses to hemorrhage and volume expansion also are preserved. During hemorrhage, this preserved response is probably related to decreases in arterial pressure and recruitment of sinoaortic baroreflexes. We hypothesize that the mechanism responsible for our findings is destruction of sensory endings that are preferentially distributed in the inferoposterior wall of the left ventricle.

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Baroreflexes and Chronic Myocardial Infarction

Minisi and Thames


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