Mechanism of biphasic response of renal nerve activity during acute cardiac tamponade in conscious rabbits

MASANOBU HAGIIKE,1,2 HAJIME MAETA,1 HIROSHI MURAKAMI,3 KENJI OKADA,2 AND HIRONOBU MORITA2
Departments of 1Surgery and 3Physiology, Kagawa Medical University School of Medicine, Kagawa 761-0793; and 2Department of Physiology, Gifu University School of Medicine, Gifu 500-8705, J apan

Hagiike, Masanobu, Hajime Maeta, Hiroshi Murakami, Kenji Okada, and Hironobu Morita. Mechanism of biphasic response of renal nerve activity during acute cardiac tamponade in conscious rabbits. Am. J. Physiol. 276 (Regulatory Integrative Comp. Physiol. 45): R1232–R1240, 1999.—Renal sympathetic nerve activity (RSNA) responses to acute cardiac tamponade were studied in conscious rabbits with all reflexes intact (Int) or after either surgical sinoaortic denervation (SAD) or administration of intrapericardial procaine (ip-Pro) or intravenous procaine (iv-Pro). In Int rabbits, the mean arterial pressure (MAP) remained relatively constant until the pericardial volume reached 7.7 ml, whereas the RSNA increased to 226% [compensated cardiac tamponade (CCT)], then, at a pericardial volume of 9.3 ml, the MAP fell sharply and RSNA decreased to 34% [decompensated cardiac tamponade (DCT)]. In Int rabbits, the RSNA increased to 226% [compensated cardiac tamponade (CCT)], then, at a pericardial volume of 9.3 ml, the MAP fell sharply and RSNA decreased to 34% [decompensated cardiac tamponade (DCT)]. 1 min after cessation of pericardial infusion, an intravenous injection of naloxone resulted in increases in both MAP and RSNA. In SAD rabbits, RSNA did not alter throughout CCT and DCT, but increased on injection of naloxone. In ip-Pro rabbits, RSNA increased during CCT but did not decrease during DCT, whereas, in iv-Pro rabbits, the RSNA response was similar to that in Int rabbits. These results indicate that RSNA responses to cardiac tamponade are biphasic, with an increase during CCT and a decrease during DCT. Sinoaortic baroreceptors are involved in mediating the increase in RSNA, whereas cardiac receptors may be involved in mediating the decrease in RSNA. An endogenous opioid may be responsible for the decrease in RSNA seen during DCT.

sinoaortic denervation; cardiac denervation; naloxone

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

METHODS

All experiments were performed on 35 chronically instrumented conscious male Japanese white rabbits weighing 2.7–3.2 kg. The study was conducted in accordance with the “Guiding Principles for Care and Use of Animals in the Field of Physiological Science” of the Physiological Society of Japan. Animals were anesthetized with pentobarbital sodium after induction with a cocktail of anesthetics (intramuscular xylazine, chlorpromazine, and ketamine), and endotra-
cheil sac was inserted for artificial ventilation. The pericardial
space was exposed through a left thoracotomy via the
fourth intercostal space, then a Silastic catheter, with two
distal side holes and connected to polyvinyl tubing (5-Fr),
was inserted into the pericardial space through a small incision
that was then closed using a purse-string suture. The catheter
and pericardium were carefully checked for leakage by
acute injection of 5 ml of sterile saline. The dead space of the
pericardial catheter was then filled with heparinized saline,
the catheter was exteriorized through the back of the neck,
and the incision was closed. After the operation, antibiotics
(15,000 U im penicillin G; Banyu, Tokyo, J apan) were given
and the animal's condition was checked daily.

Four to five days after pericardial catheter implantation,
the second operation, implantation of renal nerve electrodes,
was performed under pentobarbital sodium anesthesia (30
mg/kg iv). The left or right kidney was exposed through a
retroperitoneal flank incision, and a renal nerve bundle from
the aortic renal ganglion was dissected free from the sur-
rrounding tissue. Two stainless steel electrodes (no. 7935; A-M
Systems) were placed around it, and the nerve and electrodes
were fixed together with silicone gel (Sensocili 932 A and B;
Wacker-Chemie, Munich, Germany). The electrodes were
then exteriorized through the back of the neck, and the
incision was closed. Catheters were inserted into the thoracic
aorta and superior vena cava via the subclavian artery and
external jugular vein to measure the AP and drug injection,
respectively.

A minimum of 2 days after electrode implantation, the
tamponade experiment was carried out on the conscious
rabbit. The AP was measured by connecting the previously
implanted catheter to a pressure transducer (model TP-101T;
Nihon Kohden, Tokyo, J apan), and the heart rate (HR) was
measured using a cardiotachometer (model AT-601G; Nihon
Kohden) triggered by pulse pressure. During the progressive
cardiac tamponade, the HR was not triggered by the pulse
pressure, because the pulse pressure decreased and was
therefore counted directly from the pressure wave. An elec-
tronic R-C filter with a 2-s time constant was used to
determine the mean AP (MAP). RSNA was recorded after
amplifying the original renal nerve signal with a differential
amplifier using a band-pass filter of 30 Hz to 1 kHz (model
AVB-10; Nihon Kohden), and monitored using an oscilloscope
(model VC-10; Nihon Kohden) and audio speaker. The output
from the amplifier was passed through a gate circuit to
remove baseline noise, and the output from the gate circuit
was rectified by an absolute value circuit and integrated
using an R-C filter (50 ms). To quantify RSNA, RSNA during
the 30 s just before the tamponade experiment was defined as
100%. MAP, HR, and RSNA were sampled using an analog-to-
digital converter (MacLab/8) at a rate of 100 samples/s. After
the stabilization of all measured variables, a 5-min control
period was begun. A 10-s averaged value (1,000 points) was
used for the data at a given intrapericardial volume. For
MAP, HR, and RSNA, no difference was seen among three
time points during this control period and the averaged data
for these three points were used as the control value. Cardiac
tamponade was produced by step infusion of warmed sterile
saline into the pericardial space via the previously implanted
pericardial catheter. The rate of infusion for the first 6 ml was
2 ml/30 s; it was then changed to 1 ml/30 s until the MAP fell
below 50 mmHg (DCT). To investigate whether an endog-
enuous opioid mechanism was involved in the decrease in
RSNA seen during DCT, after a 1-min observation of DCT, we
injected a bolus dose of naloxone (3 mg/kg) intravenously (Int;
n = 7). This dose of naloxone was chosen because it had no
effect on the basal level of MAP, HR, or RSNA and was

sufficient to restore the fall in MAP and RSNA seen during
hypotensive hemorrhage to normal values (22, 28). In five
other rabbits, the effects of increased intrapericardial volume
on intrapericardial pressure (ipP) and central venous pres-
sure (CVP) were examined, but RSNA was not measured.

To investigate afferent mechanisms, i.e., the role of sinoaor-
tic baroreceptors and cardiac receptors in response to cardiac
tamponade, the same experiment was performed on SAD (n =
7), ip-Pro (n = 8), or iv-Pro (n = 6) rabbits.

SAD was performed 2 wk before the cardiac tamponade
experiment by bilateral cervical section of the aortic nerves
and stripping of the carotid sinuses while rabbits were under
pentobarbital sodium anesthesia; 7 and 12 days later, the
pericardial catheter and renal nerve electrodes, respectively,
were implanted. Completeness of SAD was confirmed before
the experiment by testing the baroreceptor-HR reflex; phentol-
ephrine (10 µg/kg iv) increased the MAP by 34 ± 11 mmHg
without any effect on HR (−3 ± 3 beats/min), and nitroprus-
toside sodium (20 µg/kg iv) decreased MAP by 53 ± 18 mmHg
without any effect on HR (−6 ± 4 beats/min). Because it was
easier to decrease the MAP in SAD rabbits compared with Int
rabbits, a different rate of pericardial infusion of 2 ml/30 s
was used for the first 2 ml, followed by 1 ml/30 s until DCT.
After a 1-min observation of DCT, a bolus dose of naloxone (3
mg/kg iv) was injected.

In eight rabbits, cardiac afferent blockade was performed
by intrapericardial infusion of 2% procaine (1 ml) (2, 8, 9).
Before starting the tamponade experiment, we confirmed
the completeness of cardiac afferent blockade by using the Bezold-
d-J arisch reflex (20 µg/kg veratridine intrapericardially); be-
fore procaine injection, the MAP and HR decreased by 24 ±
4 mmHg and 32 ± 5 beats/min, respectively, and these
responses were abolished after procaine injection (+2 ± 1
mmHg, +3 ± 2 beats/min). The cardiac tamponade exper-
iment was performed in the same way as in Int rabbits. In two
other rabbits, the effects of procaine were studied for 20 min.
During this period, the CVP and RSNA were not altered
(CVP, +0.5 mmHg; RSNA, +2.2%); the MAP increased by
13 mmHg; the HR showed a biphasic response, decreasing by
25 beats/min at 2 min after injection then gradually increas-
ing by 37 beats/min at 20 min; the Bezold-J arisch reflex was
completely abolished from 2 to 20 min after procaine injec-
tion; no respiratory incoordination was seen; and arterial
blood oxygen saturation, measured using a pH-blood gas
analyzer (model Stat PO 5; Nova Biomedical, Newton, MA),
was maintained at >97%. To exclude effects of leakage of
procaine into peripheral vasculature in ip-Pro rabbits, the
same experiment was performed after iv-Pro administration
(1 ml 2% procaine).

At the end of the experiment, the rabbits were killed by
anesthetic overdose, and a necropsy was performed to confirm
the positioning of the pericardial catheter and the absence of
leakage.

Statistical analysis. All values are presented as means ±
SE. In Table 1, the pericardial volume was analyzed by
one-way ANOVA, with the groups of animals as a factor (Int,
SAD, ip-Pro, and iv-Pro). MAP, HR, and RSNA were analyzed
by two-way ANOVA, with conditions of cardiac tamponade
and groups of animals as two factors, followed by post hoc
comparison of Fisher's protected least significant difference.
The effects of ip-Pro and iv-Pro to MAP, HR, and RSNA were
compared with the preinjection level using Student's paired
t-test. In all tests, a P value <0.05 was considered statisti-
cally significant.
RESULTS

The effects of the increased pericardial volume on ipP, CVP, MAP, and HR in the five ipP-CVP rabbits were summarized in Fig. 1. During cardiac tamponade, both the ipP and CVP increased in proportion to the pericardial volume ($y = 0.24x$, $r = 0.986$ and $y = 0.46x + 2.7$, $r = 0.934$, respectively). In contrast, the changes in MAP and HR were not a linear response.

Figures 2–4 show the original recording illustrating typical AP, RSNA, and integrated RSNA responses to cardiac tamponade in one Int, SAD, and ip-Pro rabbit, respectively.

For the Int rabbits, the averaged data (Fig. 5) show that the MAP was maintained relatively constant at about 80 mmHg until the pericardial volume increased to 7.7 ± 0.5 ml, then fell abruptly to 44 ± 2 mmHg at a pericardial volume of 9.3 ± 0.4 ml. As the intrapericardial volume increased to 7.7 ± 0.5 ml, the HR increased from 221 ± 7 to 311 ± 17 beats/min, but a further increase in intrapericardial volume resulted in an abrupt fall in HR to the control level. RSNA increased with increasing intrapericardial volume up to 226 ± 24% at a volume of 7.7 ± 0.5 ml, then decreased to below the control level as the intrapericardial volume continued to increase. Responses of iv-Pro rabbits were similar to those in Int rabbits (Fig. 5).

In contrast, the averaged data for the SAD rabbits (Fig. 5) show that the MAP gradually decreased as the intrapericardial volume increased, whereas the HR and RSNA did not alter significantly throughout the tamponade period.

In ip-Pro rabbits, the MAP stayed relatively constant around the control level until the pericardial volume increased to 7.6 ± 0.6 ml, then fell abruptly to 45 ± 1 mmHg at an intrapericardial volume of 9.6 ± 0.8 ml.

Table 1. Changes in variables during cardiac tamponade

<table>
<thead>
<tr>
<th>Pericardial volume, ml</th>
<th>Preinjection of Procaine</th>
<th>Control</th>
<th>CCT</th>
<th>DCT</th>
<th>Naloxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Int</td>
<td>0</td>
<td>7.7 ± 0.5</td>
<td>9.3 ± 0.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAD</td>
<td>0</td>
<td>4.4 ± 0.7†</td>
<td>6.4 ± 0.7†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ip-Pro</td>
<td>0</td>
<td>7.6 ± 0.6</td>
<td>9.6 ± 0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iv-Pro</td>
<td>0</td>
<td>7.5 ± 0.8</td>
<td>9.5 ± 0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Int</td>
<td>78 ± 4</td>
<td>67 ± 4</td>
<td>44 ± 2*</td>
<td>90 ± 4</td>
<td></td>
</tr>
<tr>
<td>SAD</td>
<td>85 ± 4</td>
<td>69 ± 4*</td>
<td>44 ± 2*</td>
<td>90 ± 14</td>
<td></td>
</tr>
<tr>
<td>ip-Pro</td>
<td>77 ± 6</td>
<td>90 ± 7‡</td>
<td>78 ± 7</td>
<td>45 ± 1*</td>
<td>(0, +4) from DCT</td>
</tr>
<tr>
<td>iv-Pro</td>
<td>77 ± 2</td>
<td>82 ± 3</td>
<td>69 ± 2</td>
<td>44 ± 2*</td>
<td>81 ± 6</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Int</td>
<td>221 ± 7</td>
<td>311 ± 17*</td>
<td>246 ± 15</td>
<td>216 ± 15</td>
<td></td>
</tr>
<tr>
<td>SAD</td>
<td>265 ± 14</td>
<td>260 ± 15</td>
<td>259 ± 13</td>
<td>212 ± 8*</td>
<td></td>
</tr>
<tr>
<td>ip-Pro</td>
<td>233 ± 11</td>
<td>255 ± 13</td>
<td>277 ± 18</td>
<td>281 ± 18</td>
<td>(−12, −6) from DCT</td>
</tr>
<tr>
<td>iv-Pro</td>
<td>225 ± 15</td>
<td>228 ± 17</td>
<td>299 ± 11*</td>
<td>257 ± 23</td>
<td>208 ± 18</td>
</tr>
<tr>
<td>RSNA, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Int</td>
<td>100 ± 4</td>
<td>226 ± 24*</td>
<td>34 ± 12*</td>
<td>301 ± 36*</td>
<td></td>
</tr>
<tr>
<td>SAD</td>
<td>99 ± 8</td>
<td>83 ± 17†</td>
<td>77 ± 8</td>
<td>251 ± 44*</td>
<td></td>
</tr>
<tr>
<td>ip-Pro</td>
<td>96 ± 11</td>
<td>99 ± 3</td>
<td>271 ± 55*</td>
<td>333 ± 84†</td>
<td>(–40, –104) from DCT</td>
</tr>
<tr>
<td>iv-Pro</td>
<td>106 ± 15</td>
<td>103 ± 5</td>
<td>241 ± 38*</td>
<td>25 ± 10*</td>
<td>290 ± 25*</td>
</tr>
</tbody>
</table>

Values are means ± SE; intact rabbits (Int), $n = 7$; sinoaortic-denervated rabbits (SAD), $n = 7$; intrapericardial procaine rabbits (ip-Pro), $n = 8$; intravenous procaine rabbits (iv-Pro), $n = 6$. MAP, mean arterial pressure; HR, heart rate; RSNA, renal sympathetic nerve activity; CCT, compensated cardiac tamponade; DCT, decompensated cardiac tamponade. *$P < 0.05$; significantly different from control, †$P < 0.05$; significantly different from preinjection of procaine at paired $t$-test.
whereas the HR did not alter throughout the tamponade period. In contrast to Int rabbits, RSNA in ip-Pro rabbits increased continuously, reaching $333 \pm 84\%$ at $9.6 \pm 0.8$ ml, although the MAP had decreased to $45 \pm 1$ mmHg at this point. In four animals in this group, tamponade experiments were repeated on the next day without the use of ip-Pro and the biphasic RSNA response was again found to be present.

For the among-groups comparison, the cardiac tamponade was divided into two stages: CCT, defined as the
maximal pericardial volume at which the MAP was maintained at a value \( \geq 80\% \) of the control value; and DCT, defined as the minimum pericardial volume at which the MAP fell below 50 mmHg. The statistical results, summarized in Table 1, show a significant difference in pericardial volume as a factor of the group of animals (\( P < 0.0001 \)), with the pericardial volumes for CCT and DCT in SAD rabbits being significantly lower than those in Int rabbits, whereas the intrapericardial volumes for CCT and DCT in ip-Pro and iv-Pro rabbits (including 1 ml of procaine in ip-Pro rabbits) were similar to those in Int rabbits. In ip-Pro and iv-Pro rabbits, the values for the MAP and HR were significantly different as a factor of the tamponade condition (\( P < 0.0001 \) and \( P < 0.001 \), respectively). In Int and iv-Pro rabbits, the HR increased significantly during CCT then decreased to the control level during DCT; the increase in HR during CCT was completely abolished by SAD or ip-Pro. In terms of RSNA, there was a significant difference for two factors (tamponade condition, \( P < 0.0001 \); groups of animals, \( P < 0.001 \)). In Int and iv-Pro rabbits, the RSNA responses to cardiac tamponade were biphasic; i.e., they increased significantly during CCT then decreased below the control level during DCT. In contrast, in ip-Pro rabbits, RSNA increased during CCT, but the decrease during DCT was completely abolished, and, in SAD rabbits, both the increase during CCT and the decrease during DCT were abolished.

After an observation period of at least 1 min of DCT, naloxone was injected (Fig. 6 and Table 1). In Int, iv-Pro, and SAD rabbits, the MAP increased to the control level and the RSNA increased to a value well above the control level, whereas the HR did not alter in Int and iv-Pro rabbits but significantly decreased in SAD rabbits. When naloxone was injected into two ip-Pro rabbits during DCT, no reproducible improvement in hemodynamics and RSNA was seen. In one, the MAP remained at 35 mmHg and RSNA altered from 285% during DCT to 325%, whereas, in the other, the MAP and RSNA altered from 48 to 52 mmHg and from 860 to 756%, respectively. Both rabbits struggled violently after naloxone injection and died, so no other ip-Pro rabbits were given naloxone.

**DISCUSSION**

The major findings of the present study are that 1) in Int conscious rabbits, the RSNA response to acute cardiac tamponade is biphasic, showing an increase during CCT and a decrease during DCT; 2) sinoaortic baroreceptors are involved in an afferent mechanism mediating the increase in RSNA, whereas cardiac receptors may be involved in an afferent mechanism mediating the decrease in RSNA; and 3) endogenous opioid may be one of the mechanisms involved in the decrease in RSNA during DCT.

Since the 1980s, the ip-Pro technique has been used by many investigators to block the cardiac nerve (2, 8, 9). In the present study, cardiac afferent blockade was confirmed by the absence of the Bezold-Jarisch reflex. Although efferent blockade was not directly confirmed,
this might reasonably be assumed to be the case, because higher concentrations of procaine are required to produce cardiac afferent blockade compared with efferent blockade (2, 29). In fact, the HR in ip-Pro rabbits did not alter during the experiment and cardiac contractility might not be increased because epicardial procaine abolished responses of cardiac contractility induced by electrical stimulation of sympathetic and parasympathetic efferents (1). These hemodynamic changes due to cardiac efferent blockade may therefore indirectly influence the RSNA response to cardiac tamponade.

A biphasic RSNA response has been reported in conscious dogs and rabbits during hemorrhage (3, 24), with RSNA increasing during nonhypotensive hemorrhage and decreasing during hypotensive hemorrhage. The increase in RSNA is mediated by both sinoaortic baroreceptors and cardiac receptors because, in conscious dogs, neither SAD nor cardiac denervation alone is sufficient to block the increase, whereas SAD plus vagotomy completely abolishes the increase (24). In conscious rabbits, the increase in RSNA is mediated mainly by sinoaortic baroreceptors (19, 31). However, the afferent pathway of the RSNA decrease is controversial (31). Morita and Vatner (24) reported that in conscious dogs the RSNA decrease is not affected by

---

**Fig. 5.** Averaged data for MAP, HR, and RSNA during cardiac tamponade. ○, Int rabbits (n = 7); ●, SAD rabbits (n = 7); ▽, ip-Pro rabbits (n = 8); ▼, intravenous procaine-treated rabbits (iv-Pro, n = 6). Six data points for Int and iv-Pro rabbits indicate averaged data for control values and those at an intrapericardial volume of 2, 4, or 6 ml and during compensated cardiac tamponade (CCT) and decompen-sated cardiac tamponade (DCT). Five points for SAD rabbits indicate averaged data for control values and those at an intrapericardial volume of 2 or 3 ml and during CCT and DCT. Five points for ip-Pro rabbits indicate averaged data for control values and those at an intrapericardial volume of 3 or 5 ml and during CCT and DCT.

---

**Fig. 6.** Averaged data for MAP, HR, and RSNA after naloxone (3 mg/kg) administration. ○, Int rabbits (n = 7); ●, SAD rabbits (n = 7); ▽, iv-Pro rabbits (n = 6).
surgical cardiac denervation or SAD plus vagotomy. In contrast, Burke and Dorward (3) reported that in conscious rabbits the RSNA decrease is completely abolished by ip-Pro. The discrepancy might be due to species differences (31) and/or differences in cardiac denervation methodology. In both studies, the RSNA decrease was reversed by naloxone, indicating that endogenous opioid is one mechanism involved in the RSNA decrease occurring during hypotensive hemorrhage (3, 28). This is also the case in the present study, because the decreases in MAP and RSNA during DCT were reversed by naloxone. Thus endogenous opioid may be responsible for the decrease in RSNA during DCT.

In anesthetized dogs, conflicting results have been reported for the RSNA response during cardiac tamponade, with Osborn and Lawton (27) reporting that RSNA increases continuously during cardiac tamponade and Shibamoto et al. (32) reporting a biphasic RSNA response during cardiac tamponade. This discrepancy might be due to the MAP reached during cardiac tamponade because, in the former study, the MAP decreased from 125 to 82 mmHg and RSNA increased to 240%, whereas, in the latter study, the MAP and RSNA decreased to 50 mmHg and 77%, respectively. In the present study, the MAP also decreased to 50 mmHg, but the magnitude of the RSNA response was greater, with a decrease to 34%, almost the same as the noise level (in 3 of 7 rabbits, RSNA was completely inhibited). This difference is probably due to the effect of anesthesia and acute surgical stress. It is known that pentobarbital sodium anesthesia produces a decrease in RSNA in SAD animals; however, if the baroreflex system is intact, RSNA recovers to the control level or slightly increases (20, 23). Thus pentobarbital sodium anesthesia modifies the baroreflex system and the baseline RSNA level. The other possibility is that the autonomic nervous system in anesthetized acutely prepared animals is already modified by endogenous opioid released by anesthesia and surgical stress. Smith et al. (33) demonstrated that acute surgical stress causes a more than fivefold increase in plasma β-endorphin levels. In addition, in anesthetized cats, naloxone increases the MAP and sympathetic nerve activity (16), whereas, in conscious rabbits, it has no significant effect on MAP or RSNA if there has been no previous blood loss (28). Thus it is possible that the sympathetic nervous system in anesthetized acutely prepared animals is already modified by endogenous opioid.

The most important difference between cardiac tamponade and hemorrhage is whether the total blood volume changes. Hemorrhage results in a decrease in total blood volume, venous return, atrial pressure, ventricular filling, cardiac output, and MAP. Both sinoaortic baroreceptors and cardiac receptors are unloaded, and the increase in RSNA is mediated by these receptors (5, 24). In contrast, cardiac tamponade does not decrease the total blood volume, whereas the increased ipP impairs cardiac filling and decreases cardiac output and MAP. Atrial pressure is reported to increase during cardiac tamponade (15); however, cardiac receptors may not be stimulated for the following reasons. First, the calculated atrial transmural pressure is not increased, but actually decreases, despite an increased atrial pressure (15). Second, echocardiography shows that the atrium is not distended during cardiac tamponade (12). Third, plasma atrial natriuretic peptide levels are decreased by cardiac tamponade (14). Accordingly, cardiac receptors may not be stimulated, but remain unaffected or unloaded during cardiac tamponade. Thus the input from sinoaortic baroreceptors and cardiac receptors during cardiac tamponade is similar to that during hemorrhage and/or vena caval occlusion (18).

The RSNA increase during CCT was completely abolished by SAD, indicating that it is mediated by sinoaortic baroreceptors but not by cardiac receptors. In contrast, the decrease in RSNA during DCT was completely abolished by ip-Pro. According to this result and those reported from other studies on hemorrhage and vena caval occlusion (3, 10, 19), the decrease in RSNA seen during DCT might be mainly mediated by the cardiac nerves. The decreases in MAP and RSNA seen during DCT in Int rabbits were reversed by intravenous naloxone injection. In the two ip-Pro rabbits tested, the MAP was not increased by naloxone. These results indicate that the cardiac nerve-mediated endogenous opioid secretion occurred during DCT, in agreement with results on hemorrhagic hypotension showing that cardiac receptors have an opiate synapse on their reflex pathways to the renal nerve (3) and that an endogenous opioid mechanism is located within the central nervous system (10, 36). In our own unpublished work, methyl-naloxone, which does not pass the blood-brain barrier, had no effect on RSNA during DCT, suggesting that a central opioid mechanism is also involved in the decrease in RSNA during DCT.

In SAD rabbits, RSNA was not altered by cardiac tamponade during either CCT or DCT. This suggests that sinoaortic baroreceptors may be involved not only in the increase, but also the decrease, in RSNA. Ludbrook and Ventura (19) examined hemodynamic responses to inferior vena caval occlusion and showed that the abrupt increase in systemic vascular conductance; i.e., “sympathoinhibition,” occurs by caval occlusion in the Int rabbit but it does not occur in the absence of cardiac receptor input or sinoaortic baroreceptor input. Their results support the above-mentioned possibility. However, naloxone increased the MAP and RSNA during DCT in SAD rabbits, indicating that endogenous opioid should be secreted during DCT. Thus it is also possible that, in SAD rabbits, an increase in endogenous opioid levels attempted to decrease RSNA but failed to do so or that the decrease was not observed; in this context, it is interesting to note that detection of the sympathoinhibitory phase is difficult if there is no previous sympathoexcitatory phase (31). In the present study, in SAD rabbits, RSNA during DCT tended to decrease, although this effect did not reach statistical significance. Further investigations are required to clarify these possibilities.
Perspectives

The term sympathoinhibition is based on the decrease in RSNA and the limiting of the plasma norepinephrine concentration during hypotensive hemorrhage and DCT (3, 24, 30, 31). The physiological and/or pathophysiological significance of sympathoinhibition caused by endogenous opioid is still unclear, and it is not known whether it has beneficial or deleterious effects on the animal. One benefit is considered to be that, when faced with reduced ventricular filling, sympathoinhibition prevents cardiac overload by its effects on the ventricular muscle and peripheral arterioles, i.e., reduced cardiac contractility and afterload (4, 31). The question can be raised whether cardiac sympathetic nerve activity decreases during the sympathoinhibitory phase. Unfortunately, no data are available from conscious animals; however, in anesthetized animals, cardiac sympathetic nerve activity remains elevated during hypotensive hemorrhage and DCT (17, 32). Regional differences in sympathetic nerve activity are well documented (17, 34). It is possible that cardiac sympathetic nerve activity would not decrease in the sympathoinhibitory phase. If this were the case, we would have to consider the significance for the kidney of the RSNA decrease. The renal sympathetic nerve controls sodium and water reabsorption by effects on renin secretion, by direct effects on tubular reabsorption of sodium, and by altering renal hemodynamics (7). During CCT, the increased RSNA acts on sodium and water reabsorption to maintain the blood volume and AP. However, during DCT, if RSNA remains elevated, it is difficult to maintain a minimal urine volume in the face of decreased AP. Thus the decrease in RSNA during DCT may have a beneficial effect in maintaining a minimal urine volume and preserving renal function.

This study was supported in part by a research grant from the Ministry of Education, Science and Culture of Japan (nos. 09470008 and 10671262). Address for reprint requests and other correspondence: M. Hagiike, Dept. of Surgery, Kagawa Medical Univ. School of Medicine, Kagawa 761-0793, Japan.

Received 17 February 1998; accepted in final form 12 January 1999.

REFERENCES


