Comparison of Afferent Activity of Canine Aortic and Sinus Nerves

By Conrad L. Pelletier, Denis L. Clement, and John T. Shepherd

ABSTRACT

Pressure-dependent changes in afferent activity in the aortic and the sinus nerves were studied in 17 anesthetized dogs that were artificially ventilated with oxygen. Systemic arterial blood pressure was varied either continuously or in steps over the range of mean aortic blood pressure from 220 to 50 mm Hg with a pressurized reservoir connected to the abdominal aorta. Multifiber preparations from 20 aortic and 8 sinus nerves were used, and stimulus-response curves were defined by measuring the mean impulse frequency at the various levels of pressure. Heart rate and pulse pressure were similar during recordings from both nerves. The two curves were S-shaped, with that for the aortic nerve being to the right of that for the sinus nerve. The change in activity was approximately linear from 200 to 120 mm Hg (mean aortic blood pressure) in the aortic nerve and from 180 to 80 mm Hg in the sinus nerve; there was no significant change in impulse frequency below mean blood pressures of 100 and 70 mm Hg, respectively. The threshold systolic blood pressure was 95 ± 3 (SE) mm Hg for the aortic receptors and 62 ± 4 mm Hg for the carotid sinus receptors. Thus, in the dog, the aortic baroreceptors are involved mainly in the control of high blood pressure, whereas at lower pressures the major control occurs through the carotid sinus baroreflex.

KEY WORDS

blood pressure control     baroreceptor    stimulus-response analysis
baroreceptor              depressor nerve  electroneurograms

The carotid sinus baroreceptors exert a more powerful buffering action on the circulation than do the aortic arch receptors (1). Until recently, this observation remained unexplained, chiefly because the technical difficulties involved in the isolation of the aortic arch precluded a detailed analysis of the aortic baroreflex. Recent investigations suggest that, in the dog, the stretch receptors of these two areas differ in their threshold and sensitivity (2, 3). Those studies, based on the cardiovascular effects of the aortic baroreflex, involved extensive surgical preparations. The manipulations around the aortic arch, the changes in physical properties of the aortic wall due to thoracotomy, and the use of nonpulsatile pressure might account, at least partly, for the differences noted between the two sets of receptors (4).

By recording afferent activity from the aortic and sinus nerves in the present experiments, the characteristics of the responses of the receptors to changes in blood pressure were studied with pulsatile pressures in the closed-chest dog. Analysis of the function of the baroreflexes by this technique required the use of multifiber preparations because of recruitment of different receptors with increasing blood pressure (5, 6). Multifiber preparations of the aortic nerve were obtained by a technique of dissection described previously (7), and the changes in afferent activity with blood pressure were compared with those of the sinus nerve.

Methods

Preparation.—Seventeen dogs, weighing 15–25 kg, were anesthetized with thiopental and...
chloralose (15 and 80 mg/kg, iv, respectively) and artificially ventilated with oxygen at 18–20 cycles/min. Additional doses of chloralose (10 mg/kg, iv) were administered regularly to maintain an even plane of anesthesia. Prior to blood vessel cannulation, heparin and gallamine triethiodide (3 mg/kg, iv, each) were administered, and these drugs were given hourly thereafter in smaller doses (1 mg/kg). At the beginning of the experiment, atropine sulfate (0.2 mg/kg, iv) was administered or the vagosympathectic trunks were cut in the neck. The arterial Po2 was maintained above 500 mm Hg and the Pco2 below 35 mm Hg; bicarbonate was administered regularly to maintain the arterial pH above 7.40.

Control of Aortic Blood Pressure.—Mean and pulsatile arterial blood pressures were measured by strain-gauge transducers (Statham P23De) via a catheter introduced into the aortic arch through the right brachial artery and recorded on an ultraviolet Visicorder (Honeywell 1508).

Large-bore cannulas introduced cephalad and caudad in the abdominal aorta below the renal arteries were connected to a pressurized reservoir. To increase the buffering effect, two large bottles (40 liters) were connected to the top of the reservoir. The air pressure in this system determined the level of mean aortic blood pressure which could be controlled to within 5 mm Hg. Because of the distal site of the aortic cannulation, central arterial blood pressure remained pulsatile. A heat exchanger incorporated in the reservoir maintained the temperature of the blood at 37°C.

Recording of Neurograms.—Afferent activity was recorded from the aortic and the carotid sinus nerves. The nerves were prepared using a dissecting microscope. The aortic nerve was identified just below the origin of the cranial laryngeal nerve from the vagus and dissected from the main trunk of the vagus (7). The nerve dissection was carried over a length of 2–3 cm, and the cephalad extremity was cut. The carotid sinus nerve was located by following the glossopharyngeal nerve to its junction with the sinus nerve. The latter was dissected for a length of about 1 cm and cut at its cephalad end. Each nerve was freed from its outer sheath and placed on a pair of platinum electrodes spaced 3–5 mm apart. The whole preparation was immersed in mineral oil to prevent drying of the nerve fibers.

The nerve signals were amplified (preamplifier A-105 and amplifier A-103/B, Lexington Instruments Corporation) and transformed into standard pulses. The standardized pulses were counted by a spike-frequency meter, and mean frequency was integrated over 5-second periods at 5-second intervals. A discriminator, used to filter noise, was set at the beginning of each recording. The time-response characteristics of the equipment permitted counting of signals occurring at intervals of 0.25 msec and greater.

Stimulus-Response Curves.—Mean afferent activity was measured from multifiber preparations of aortic and carotid sinus nerves while mean aortic blood pressure was varied over the range of 220 to 50 mm Hg. The changes in blood pressure were effected in two ways. In some experiments, mean aortic blood pressure was decreased from 220 to 50 mm Hg by successive steps of 10 or 20 mm Hg. At each level, the blood pressure was kept stable for 45–60 seconds. The initial 20 seconds was allowed to permit stabilization of nerve activity before measurements were made. This time interval was sufficient for adaptation of the receptors at the new level of pressure (6). At each pressure, 3–5 counting periods were obtained. The full range of blood pressures usually was covered within 12 minutes. In other experiments, neurograms were recorded during continuous changes in aortic blood pressure. The blood pressure was either decreased or increased at a constant speed over the range of 220 to 50 mm Hg within a period of 150–180 seconds.

Since total nerve activity varied from one preparation to another depending on the number of fibers, the results were standardized by expressing the changes in nerve traffic as a percent of the maximal activity recorded for each set of observations in the same preparation. Maximal traffic did not necessarily indicate saturation of the nerve fibers but was determined by the highest mean blood pressure that could be reached. Stimulus-response curves were defined by plotting nerve activity as impulses per second or as percent of maximal traffic against mean aortic blood pressure. In each dog, several determinations were made at each blood pressure step and averaged; this average was used to establish the mean curve for the group. The range of maximal sensitivity was defined as that portion of the curve where the relationship between mean impulse frequency and mean aortic blood pressure was approximately linear. The threshold systolic blood pressure was determined by measuring the systolic blood pressure at which the bursts of impulses ceased.

Because the dissection of the carotid sinus nerve could have damaged the carotid body, the integrity of the carotid chemoreceptors was tested at the end of the experiment by the injection of 1 mg of sodium cyanide into the common carotid artery. A massive increase in nerve activity proved that the carotid body was functional in all dogs tested. Thus, both aortic and carotid sinus chemoreceptor cells were intact.

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Results

Afferent Activity of Aortic Nerve.—Changes in aortic nerve impulse frequency with step decreases in mean aortic blood pressure were studied in 20 aortic nerves (16 left and 4 right) from 17 dogs. The maximal nerve activity (100%) was $327 \pm 23$ (se) impulses/sec at a mean aortic blood pressure of $215 \pm 2$ mm Hg. The heart rate averaged $186 \pm 6$ beats/min at this maximal mean blood pressure and $194 \pm 5$ beats/min at the minimal mean blood pressure (60 mm Hg); pulse pressure averaged $64 \pm 4$ mm Hg and $26 \pm 2$ mm Hg, respectively. An average of three series of determinations was obtained in each dog.

In the higher range of blood pressure, nerve activity was occasionally present throughout the cardiac cycle, although it was greatest during the systolic period. As aortic blood pressure decreased, both the frequency and the amplitude of the impulses decreased and activity ceased during diastole (Fig. 1). The bursts of impulses with each systolic increase in blood pressure disappeared completely.
(threshold systolic blood pressure) at a peak systolic pressure of 95 ± 3 mm Hg (range 80 to 120 mm Hg). The corresponding mean aortic blood pressure averaged 80 mm Hg (range 60 to 100 mm Hg). The average stimulus-response curve for the 20 aortic nerves is shown in Figure 2. The function curve was S-shaped, with only a slightly flattened segment above 200 mm Hg. The relationship between mean nerve activity and mean aortic blood pressure was approximately linear over the range of 200 to 120 mm Hg (range of maximal sensitivity). Below a mean aortic blood pressure of 100 mm Hg, only minimal baroreceptor activity was present, and the changes in impulse frequency were not significant.

In five of the nerves, the activity remained higher than 20% of the maximum at mean blood pressures below 100 mm Hg. In two of these nerves, both on the right side, large spikes related to inspiration were still recorded after all baroreceptor activity had ceased, and they may have been due to vagal fibers in the preparation. In another two, similar impulses were present but were not related to blood pressure or respiration; since they were abolished after a few minutes of hyperventilation, they could have been caused by chemoreceptor activity. In the other one, examination of the records showed that some noise artifact was being counted. These experiments were included in the series, even though the bottom part of the curves did not always flatten as markedly as it did in the other experiments; this may have caused a slight displacement to the left of the mean curve of the group.

In three dogs, the changes in impulse frequency in the right and left aortic nerves were compared. The shapes of the two curves were similar with only minimal changes in average activity below a mean aortic blood pressure of 100 mm Hg, although the activity remained slightly higher at low blood pressure in two of the right aortic nerves.

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

**Figure 2**

Changes in nerve activity (as percent of maximum) with step decreases in aortic blood pressure. Points are means ± SE for 20 aortic nerves from 17 dogs. Relationship between nerve activity and blood pressure was approximately linear between 200 and 120 mm Hg. The last significant change in activity occurred at a mean blood pressure of 100 mm Hg. Below this pressure, the changes in impulse frequency were not significant.
Neurograms from Aortic and Carotid Sinus Nerves.—In eight dogs, the changes in nerve activity in response to step decreases in mean blood pressure over the range of 220 to 50 mm Hg were recorded successively from the left aortic nerve and from the right (four dogs) or the left (four dogs) carotid sinus nerve. An average of three curves for each aortic nerve and two for each sinus nerve was obtained. Since, in these experiments, it was not possible to record simultaneously the activity from both nerves, the order of recordings was randomized and efforts were made to achieve similar conditions. The measurements from the two nerves were made at the same levels of mean aortic blood pressure. Heart rate and pulse pressure at the maximal and minimal levels of mean aortic blood pressure were similar during recordings from both nerves (Table 1), and no significant difference was demonstrated by Student's paired t-test (P > 0.05). The maximal impulse frequency (100%) averaged 350 ± 32 impulses/sec in the aortic nerve at a mean aortic blood pressure of 219 ± 1 mm Hg and 286 ± 38 impulses/sec in the carotid sinus nerve at a mean aortic blood pressure of 216 ± 3 mm Hg.

A typical recording from the carotid sinus nerve is shown in Figure 3. In the higher range of pressure the characteristics of carotid sinus nerve activity were similar to those of the aortic nerve, but the systolic bursts of impulses ceased at a peak systolic blood pressure (threshold) averaging 62 ± 4 mm Hg (range 40 to 75 mm Hg) compared with 98 ± 4 mm Hg for the aortic nerve in the same dogs. Threshold systolic blood pressure of the carotid sinus receptors corresponded to a mean aortic blood pressure averaging 50 mm Hg (range 40 to 60 mm Hg), whereas in the aortic nerve such activity ceased at 80 mm Hg (Fig. 4). In two carotid sinus nerves, bursts of impulses were still present during systolic upstroke at the lowest pressures studied (40 and 50 mm Hg, respectively). Paired comparison of these thresholds showed that the difference between the two nerves was significant (P < 0.001). This difference was also shown by the frequency-response curve obtained for each nerve in the same dogs (Fig. 5). The two curves were S-shaped, the curve for the aortic nerve being to the right of that for the carotid sinus nerve. Both curves flattened slightly above 200 mm Hg. The changes in nerve activity with mean blood pressure were nearly linear over the range of 200 to 120 mm Hg in the aortic nerve compared with the range of 180 to 80 mm Hg in the carotid sinus nerve. There was no further significant change in nerve activity below a mean aortic blood pressure of 100 mm Hg in the aortic nerve compared with 70 mm Hg in the carotid sinus.

| TABLE 1 | Paired Analysis of Neurograms from Aortic and Sinus Nerves in the Same Dogs |
|---------|---------------------------------|-----------------|------|
| Heart rate (beats/min) | Aortic nerve (8) | Sinus nerve (8) | P   |
| At max MBP | 187 ± 8 | 186 ± 9 | 0.8  |
| At min MBP | 202 ± 10 | 204 ± 11 | 0.7  |
| Pulse pressure (mm Hg) | | | |
| At max MBP | 67 ± 8 | 75 ± 9 | 0.2  |
| At min MBP | 25 ± 4 | 24 ± 4 | 0.4  |
| Threshold systolic blood pressure (mm Hg) | | | 0.001 |
| (range) | | | |
| At max MBP | 98 ± 4 | 62 ± 4 | 0.001 |
| At min MBP | (80–110) | (40–75) | |
| Average MBP at threshold (mm Hg) | | | 0.001 |
| (range) | | | |
| | 80 | 80 | |
| | (60–100) | (40–60) | |

Values are means ± s.e.; some ranges are indicated. MBP = mean blood pressure; max MBP = 210–220 mm Hg; min MBP = 50–60 mm Hg. P values were determined by Student's t-test. Number of dogs tested is given in parentheses.
FIGURE 3

Electroneurograms from a multifiber preparation of the right carotid sinus nerve in a dog (same dog as in Fig. 1) at various levels of aortic blood pressure, showing aortic blood pressure (A), actual traffic (AT), and standard pulse (SP). Continuous activity was present at a blood pressure of 200 mm Hg. The amplitude and the frequency of impulses decreased with decreasing pressure. The bursts of impulses during systolic upstroke persisted to the lowest pressure studied (50 mm Hg). Threshold systolic blood pressure was below 60 mm Hg.

nerve; the plateau levels of activity were 9% and 8% of maximum, respectively. The differences discussed above between the two nerves were found whether the maximal traffic was similar or different in each nerve and whether the changes were plotted in absolute values or as percents of maximum, as shown by the individual curves from four dogs (Fig. 6).

Changes in Afferent Activity during Continuous Changes in Blood Pressure.—Afferent activity was recorded from 15 aortic and 7 carotid sinus nerves during continuous changes in aortic blood pressure. The pressure was decreased and increased or increased and decreased in random order over the range of 50 to 220 mm Hg at a constant speed of about 1 mm Hg/sec. One cycle was completed in 150–180 seconds. An example of such a recording from the aortic nerve is shown in Figure 7.

The frequency-response curves were constructed by plotting the mean aortic blood pressure measured at the middle of each integration period against the mean nerve activity for this period (as percent of maximum). The many curves for each nerve were
Electroneurograms from a multifiber preparation of left aortic and right carotid sinus nerves in the same dog at the same mean aortic blood pressures. Bursts of impulses during systolic upstroke ceased in the aortic nerve at a mean blood pressure of 80 mm Hg. In the carotid sinus nerve, there was still baroreceptor activity at a mean blood pressure of 60 mm Hg. Below 100 mm Hg, there was no further change in integrated aortic nerve activity, whereas the activity of the carotid sinus nerve continued to decrease significantly. \( A \) = aortic blood pressure, \( AT \) = actual traffic, \( SP \) = standard pulse, and \( IA \) = integrated activity.

averaged to obtain a mean upward and a mean downward curve for the aortic and the carotid sinus nerves (Fig. 8). The characteristics defined by the step decreases in aortic blood pressure were also observed in these experiments. In both nerves, the impulse frequency was significantly less during the continuous decrease in pressure than it was during the continuous increase.

At a mean aortic blood pressure of approximately 100 mm Hg, aortic nerve activity was the same regardless of whether pressure was decreasing or increasing, and there was no significant change in activity at lower pressures in either situation. Above this threshold, the upward and downward curves were separated until the maximal pressure was reached. The greatest activity (100%) was obtained when the pressure was increased to 220 mm Hg; on maintaining this pressure for a few seconds, there was a 6% average decrease in traffic. By contrast, the curves obtained from the carotid sinus nerve did not overlap at any level of blood pressure. The activity continued to decrease significantly down to the lowest mean aortic blood pressure (50 mm Hg); stabilization at this pressure caused an increase in activity averaging 5%. Thus, very little flattening was observed in these curves at low aortic pressures, and significant changes in traffic occurred when mean blood pressure was changed from 50 to 70 mm Hg. On the
Comparison of stimulus-response curves from aortic and carotid sinus nerves in eight dogs. Aortic nerve curve was displaced to right of carotid sinus nerve curve. Last significant change in nerve traffic occurred at a blood pressure of 100 mm Hg for aortic nerve compared with 70 mm Hg for carotid sinus nerve. Aortic nerve curve was approximately linear over the pressure range of 120 to 200 mm Hg compared with the range of 80 to 180 mm Hg for the carotid sinus nerve curve. Both curves were only slightly flattened above 200 mm Hg.

When the curves obtained during continuous changes in aortic blood pressure were compared with those during step decreases in pressure (Fig. 5), the latter fell in between the upward and downward curves for each nerve. The difference reflected the effect of the rate of change in pressure on the baroreceptors. In the steepest part of the curves, this effect was greater for the sinus receptors than it was for the aortic receptors: in the pressure range of 140 to 150 mm Hg, the difference between the upward and the downward curves of the two nerves was 31% and 15%, respectively.

Discussion

The afferent activity originating from the arterial baroreceptors can be readily identified by its characteristic pattern (5). Preparations of single fibers or of a few fibers have been used for quantitative analysis of this activity (6, 8). When blood pressure increases, besides increased impulse frequency in each fiber, recruitment of new receptors occurs (5, 6). Such recruitment renders whole nerve or multifiber preparations necessary when total baroreceptor function is studied (9). However, quantification of the activity in a multifiber preparation is difficult due to the high impulse frequency. As the total activity increases with pressure, the amplitude of the spikes becomes larger. It has been shown using a preparation of a few fibers that spikes of different height may be obtained from different baroreceptor fibers (5, 6). In multifiber preparations, part of the larger-ampli-
Changes in mean nerve activity with changes in blood pressure in aortic and carotid sinus nerves of four dogs; integrated activity is expressed as impulses per second for each level of pressure. Aortic nerve curve was to right of carotid sinus nerve curve. Range of pressures over which the curves were linear was higher for the aortic nerve in all dogs. The aortic nerve traffic ceased to decrease at mean blood pressures of 100–110 mm Hg; carotid sinus nerve activity decreased until blood pressures of 50–70 mm Hg were reached. A difference in the maximal traffic in the two nerves (dogs C and D) did not alter these differences.

Amplitude potentials may also be caused by summation of two or more impulses occurring simultaneously (9). Since the probability of summation increases with the impulse frequency, the total activity in the higher range of pressure is likely to be underestimated compared with that in the lower range. As a result, the top part of the curve might be artificially flattened. In the present experiments, there was only a small decrease in the slope of the curves above a mean aortic blood pressure of 200 mm Hg. The bottom part of the curve would be affected minimally, since the recorded activity reached a level of less than 10% of the estimated maximum. With the technique used in this study, the function curve obtained for the carotid sinus baroreceptors was very similar to that reported by Spickler and Kezdi (10) from a computer analysis of the neurograms.

Our nerve preparations included fibers of chemoreceptive origin, and both the carotid and the aortic chemoreceptors were intact. Activity from the chemoreceptor cells was kept to a minimum by ventilating with oxygen (11, 12). To minimize the possibility of chemoreceptor activation by slight changes in $P_{CO_2}$ or pH, the dogs were hyperventilated and bicarbonate was administered regularly to maintain a slight degree of hypocapnia and alkalosis (12, 13). In the cat, decreasing the perfusion pressure of the carotid bodies may result in chemoreceptor activation due to local hypoxia; with oxygen, this effect is markedly attenuated and observed only at mean blood pressures of approximately 80 mm Hg or less.
Electroneurograms from a multifiber preparation of the left aortic nerve in a dog showing changes in mean nerve activity during continuous decrease in aortic blood pressure. Top and bottom portions of the figure are continuous. There was no change in integrated activity below a mean aortic blood pressure of 100 mm Hg, and bursts of impulses during systolic upstroke ceased. Abbreviations are the same as in Figure 4.

**Figure 8**

Stimulus-response curves obtained from 15 aortic nerves and 7 carotid sinus nerves during continuous decreases and increases (indicated by arrows) in aortic blood pressure. In both nerves, activity was significantly less during the downward curve; the difference between the two curves was larger for the carotid sinus nerve. Aortic nerve curves overlapped from a mean blood pressure of 100 mm Hg downward, and no change in activity occurred between 100 and 60 mm Hg. In contrast, carotid sinus nerve curves remained separated and showed significant changes in impulse frequency until 50 mm Hg.
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(14, 15). It is not known if the chemoreceptors are activated by hypotension in the dog. A difference in sensitivity between the aortic and the carotid sinus chemoreceptors to changes in perfusion pressure would have to be invoked to explain the difference between the curves on this basis. It would thus be unlikely that the marked flattening of the function curve of the aortic receptors below a mean aortic blood pressure of 100 mm Hg could be attributed to an activation of the chemoreceptors.

The recordings from the aortic and the carotid sinus nerves were made from the same dogs and under similar conditions of heart rate, pulse pressure, and mean aortic blood pressure. With the use of atropine or vagotomy, only a minimal increase in heart rate occurred with the decrease in aortic blood pressure. No attempts were made to maintain the pulse pressure constant, since this normally decreases when blood pressure decreases. However, the changes in pulse pressure were similar during the recordings from both nerves. Thus, a valid comparison could be made of the function curves of each receptor area. Our results demonstrate that the carotid stretch receptors have a lower threshold than do the receptors of the aortic arch and that the former system has a maximal sensitivity over a lower range of aortic blood pressure than does the latter. The differences between the two curves were not affected by plotting the nerve activity in absolute values or as percents of the maximal activity for each nerve. Analysis of the changes in impulse frequency during pressure increases or decreases at constant speed permitted an assessment of the effect of the rate of change in pressure on each group of baroreceptors. In their steepest part, the hysteresis between the carotid sinus curves was twice as large as that between the aortic curves. This suggests that the carotid sinus baroreflex is more sensitive to the rate of pressure changes than is the aortic baroreflex and corroborates the results of Irisawa and Ninomiya (16) and of Dampney et al. (17).

Earlier studies from this laboratory based on the reflex vascular responses showed that the average threshold pressure of the aortic baroreceptors was 110 mm Hg compared with 47 mm Hg for the carotid sinus baroreceptor and that the pressure of maximal sensitivity averaged 45 mm Hg higher for the former (3). Other investigators have reported similar or higher values for the aortic receptors (2, 18, 19). However, in these experiments, the effect of the surgical preparation on the aortic receptors cannot be assessed. The results of the present investigation in closed-chest dogs with intact baroreceptor areas and under the normal condition of pulsatile pressure are in accordance with the previous studies and demonstrate that the difference between the function curves of the two reflexogenic areas could not be attributed to technical factors. The nerve recordings performed during continuous changes in pressure also suggest a lower saturation pressure for the sinus receptors, as do the hemodynamic responses (3). However, the technique used to evaluate afferent activity does not permit an accurate definition of this value.

Thus, at normal blood pressure, the aortic nerve of the dog displays little activity compared with the carotid sinus nerve. This is in keeping with the findings that, in the dog, the hemodynamic adjustments to hemorrhage are achieved predominantly by the carotid sinus baroreflex (20). By contrast, in the rabbit, the aortic receptors remain active at low blood pressure, indicating species variations in the behavior of the two baroreceptor areas (21, 22). Whether the dissimilarity between the sinus and aortic reflexes of the dog reflects a difference in the receptors themselves or the fact that they are situated in vessels of different size and characteristics is not established. A difference in the total number of receptors in each area could be partly responsible for the predominance of the sinus baroreflex; however, this difference would not modify the relationship between the function curves as defined by the afferent activity in each nerve. Thus, in the dog, the carotid reflex is a true buffer system, whereas...
the aortic reflex acts predominantly as an antihypertensive mechanism.

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