Hypertension attenuates cell-to-cell communication in hamster retractor muscle feed arteries

David T. Kurjiaka,1 Shawn B. Bender,1 Darin D. Nye,1 William B. Wiehler,2 and Donald G. Welsh2

1Department of Biological Sciences, Ohio University, Athens, Ohio; and 2Department of Physiology and Biophysics, University of Calgary, Calgary, Alberta, Canada

Submitted 20 July 2004; accepted in final form 12 October 2004

Kurjiaka, David T., Shawn B. Bender, Darin D. Nye, William B. Wiehler, and Donald G. Welsh. Hypertension attenuates cell-to-cell communication in hamster retractor muscle feed arteries. Am J Physiol Heart Circ Physiol 288: H861–H870, 2005. First published October 14, 2004; doi:10.1152/ajpheart.00729.2004.—This study examined whether hypertension attenuated cell-to-cell communication in skeletal muscle resistance arteries. Briefly, arteries feeding the retractor muscle of normotensive and hypertensive hamsters were cannulated, pressurized, and superfused with a physiological saline solution. Cell-to-cell communication was functionally assessed by application of vasoactive stimuli (via micropipette) to a small portion of a feed artery while diameter at sites distal to the point of agent application was monitored. Keeping with past observations, discrete application of a smooth muscle depolarizing agent (phenylephrine or KCl) elicited a localized vasoconstriction that conducted poorly along feed arteries from normotensive hamsters. In contrast, acetylcholine, an agent known to hyperpolarize endothelial cells, elicited a vasodilation in normotensive feed arteries that conducted with little decay. Whereas smooth muscle depolarizing agents continued to elicit a localized response, conduction of endothelium-dependent vasodilation was attenuated in hypertensive hamsters. This decrease occurred in the absence of changes in vessel reactivity to intravascular pressure or to global application of phenylephrine, U-46619, or acetylcholine. We propose, on the basis of these physiological observations, quantitative mRNA measurements of connexins 37, 40, 43, and 45, and analysis of the literature, that an increase in endothelial-to-endothelial or smooth muscle-to-endothelial coupling resistance is likely responsible for hypertension-induced impairment in vascular communication. We hypothesize that this attenuation could contribute to the rise in total peripheral resistance characteristically observed in hypertension.

Vascular studies have long appreciated that cell-to-cell communication can be physiologically assessed by application of vasoactive agents to a small portion of a resistance vessel (30, 31). This discrete application of agent initiates a focal change in smooth muscle or endothelial cell membrane potential that, likely with the aid of gap junctions, conducts to neighboring vascular cells (41, 42). By monitoring the extent to which the electrical or the corresponding vasomotor response conducts along the vessel wall, the nature of cell-to-cell communication can be functionally elucidated. With this simple bioassay, past investigations have generally observed that endothelium-dependent responses robustly conduct along small arteries isolated from a variety of tissues (18, 33, 41). In contrast, the spread of smooth muscle-dependent responses varies widely, with many resistance vessels, including those from skeletal muscle, displaying little or no conduction (17, 33, 43).

Investigations of vascular communication have typically focused on defining fundamental factors that underlie this key regulator of tissue blood flow. Although essential, few studies have extended beyond this line of inquiry to address whether cell-to-cell communication could be altered by vascular disease and whether such changes could facilitate the progression of a pathophysiological state. Reason dictates that any disease state that alters coupling resistance between adjacent vascular cells should directly influence cell-to-cell communication. Despite limited examination, past investigations have raised the possibility that hypertension may be capable of elevating coupling resistance (5, 6, 11). This view has been largely predicated on 1) Cx-knockout studies, which have revealed a relation among Cx40 expression, cell-to-cell communication, and elevated blood pressure (5, 6), and 2) findings from large conduit arteries documenting the ability of hypertension to alter Cx expression and upregulate signaling proteins known to reduce gap junctional communication (3, 11, 19, 37).

This study examined whether hypertension influenced the nature of cell-to-cell communication in small skeletal muscle resistance arteries. Briefly, vascular communication was functionally examined by application of vasoactive agents (i.e., KCl, phenylephrine, and acetylcholine) to a small portion of a retractor muscle feed artery while vasomotor responses distal to the site of agent application were monitored. Consistent with past observations (41), responses originating in endothelial, but not smooth muscle, cells conducted robustly along skeletal muscle arteries from normotensive hamsters. In hypertensive hamsters, the conduction of endothelium-dependent vasodilation was attenuated, particularly in vessels preconstricted with...
a combination of intravascular pressure and superfused agonist. Interestingly, this reduction in cell-to-cell communication arose in the absence of a change in vessel reactivity to intravascular pressure or to global application of vasoactive agents. We conclude from these findings and real-time PCR measures of Cx37, Cx40, Cx43, and Cx45 mRNA that the hypertension-induced attenuation in cell-to-cell communication likely arises from an increased coupling resistance between adjacent endothelial cells or between the smooth muscle and endothelial cell layers. This decrease in vascular communication could facilitate a rise in total peripheral resistance and, thus, further the progression of the hypertensive state.

METHODS

All procedures were approved by the Animal Care and Use Committees at the University of Calgary and Ohio University. In general, normotensive (CHF-148, Canadian Hybrid Farms, Halifax NS, Canada) and hypertensive (CHF-H4) hamsters at 26 wk of age were anesthetized with pentobarbital sodium (65 mg/kg ip) and placed on a Plexiglas platform for viewing under a stereomicroscope.

Hemodynamic Measurements

To measure mean arterial blood pressure, a cannula (PE-50 tubing) was rapidly secured in the left carotid artery and connected to a pressure transducer. Hemodynamic data were collected on a MacLab data acquisition system while hamsters were maintained under light anesthesia as determined by the presence of the ear-pinch reflex. Mean arterial pressure was calculated over an average of 10 pressure pulses. After experimentation, animals were euthanized with pentobarbital sodium (130 mg/kg ip).

Feed Artery Preparation

To isolate feed arteries, an incision was made through the skin to expose the left retractor muscle. Overlying connective tissue was carefully removed while the entire preparation was superfused with a combination of intravascular pressure and superfused agonist. Interestingly, this reduction in cell-to-cell communication arose in the absence of a change in vessel reactivity to intravascular pressure or to global application of vasoactive agents. We conclude from these findings and real-time PCR measures of Cx37, Cx40, Cx43, and Cx45 mRNA that the hypertension-induced attenuation in cell-to-cell communication likely arises from an increased coupling resistance between adjacent endothelial cells or between the smooth muscle and endothelial cell layers. This decrease in vascular communication could facilitate a rise in total peripheral resistance and, thus, further the progression of the hypertensive state.

Characterizing feed artery reactivity. Vessel reactivity was characterized in normotensive and hypertensive animals by monitoring feed artery responses to intravascular pressure and to global application of vasoactive agonists. To assess myogenic tone, feed arteries were pressurized to 60 or 90 mmHg; vasomotor responses were measured and expressed as an absolute value or as a percentage of maximal diameter. Vas constrictor reactivity was examined by pressurizing feed arteries to 60 mmHg and increasing the concentration of phenylephrine or U-46619 (a stable thromboxane A2 mimetic) in the superfusate every 5 min. In contrast, the vasodilatory effects of acetylcholine were examined by first preconstricting feed arteries with intravascular pressure (60 mmHg) and phenylephrine (3 × 10⁻⁷ M in the superfusate) and then exposing the vessel to an increasing global concentration of this vasodilator every 5 min. Agonist-induced arterial responses are expressed as a percentage of vasodilator or vasoconstrictor capacity (see Statistical Analysis).

Conduction of smooth muscle-dependent responses. A micropipette filled with phenylephrine or KCl was carefully positioned with the tip adjacent to the distal end of a feed artery (Fig. 1), maintained at an intravascular pressure of 60 mmHg. With use of microiontophoresis for phenylephrine (1–3 s pulse, 1 μA ejection current, 0.2 μA retain current) or pressure ejection for KCl (1–5 s pulse, 20 psi ejection pressure), a small quantity of agent was applied to the feed artery, and vasoconstriction was evaluated 0, 450, 900, 1,350, and 1,800 μm upstream from the site of agent application. The stimulus duration was adjusted for each feed artery to elicit a vasoconstrictor response of 20–30 μM at the local application site; this represented ~40% of the vasoconstrictor capacity. When KCl micropipettes were used, care was taken to minimize pulse duration so as to prevent direct depolarization of the underlying endothelium.

Conduction of endothelium-dependent responses. After equilibration, a micropipette filled with acetylcholine, an agent that hyperpolarizes endothelial cells, was carefully positioned with the tip adjacent

![Fig. 1. Methodology used to measure cell-to-cell communication in a retractor muscle feed artery. A feed artery is cannulated, and a stimulus pipette containing vasoactive agents is placed close to the vessel. Vasoactive agents are liberated from the pipette, and arterial diameter is measured every 450 μm along the artery’s longitudinal axis (*).](http://ajpheart.physiology.org/).
to the distal end of a feed artery (Fig. 1). Acetylcholine was discretely applied to the feed artery by microiontophoresis (0.1–0.5 μA pulse, 1 μA ejection current, 0.2 μA retain current), and vasodilation was evaluated at 0, 450, 900, 1,350, and 1,800 μm upstream from the site of agent application. Conducted vasodilation was monitored in feed arteries that were constricted to 1) intravascular pressure alone (60 or 90 mmHg) or 2) intravascular pressure (60 mmHg) in combination with superfused phenylephrine (3 x 10^{-7} M) or U-46619 (3 x 10^{-9} M). The stimulus duration was adjusted for each feed artery to elicit a vasodilatory response of 25–30 μm at the local application site; this represented ∼45–60% of the vasodilatory capacity.

**Real-Time PCR Analysis**

Four to five feed arteries (3–4 mm long) from each hamster were cleaned and placed in RNase- and DNase-free collection tubes and fast frozen in liquid nitrogen. Total RNA was subsequently extracted with the RNeasy Minikit with DNase treatment (Qiagen, Valencia, CA), and first-strand cDNA was synthesized using the Sensiscript RT kit (Qiagen) with oligo(dT) primer. To optimize reaction specificity, real-time PCR was initially performed on each primer set using hamster brain cDNA, SYBR green (Bio-Rad, Hercules, CA), and a range of annealing temperatures (52–62°C). On the basis of melt-curve analysis, 1 μl of each reaction product was placed on a DNA 500 lab chip and examined using a bioanalyzer (model 2100, Agilent Technologies). A second aliquot of product was electrophoresed on a 1.5% (wt/vol) agarose gel, extracted using a gel extraction kit (Qiagen), and sequenced at the University of Calgary Core DNA facility. Having ascertained an ideal annealing temperature, real-time PCR efficiency was determined for all primer sets, with serial dilutions of brain cDNA used as template. The optimal real-time PCR consisted of a hot start (95°C for 3 min) followed by 40 cycles of 95°C for 15 s, 55.1°C for 30 s, and 72°C for 30 s. A melt-curve analysis was performed on each reaction, and the threshold cycle was determined using software provided with the Bio-Rad iCycler. Forward and reverse primers specific to rat Cx37, Cx40, Cx43, and β-actin were as follows: 5'-CGTTCGAGACCTTACC-3' (forward) and 5'-GGATGAGAGCCCATTGTAG-3' (reverse) for Cx43, 5'-CTGTATGGGATCTTCCTGGATACC-3' (forward) and 5'-CACAGCCAGCATAAAGACAATGAA-3' (reverse) for Cx45, 5'-CAAGCTGTGGATCCCGGATACC-3' (forward) and 5'-CTGTCCTGCATTGCTGCCCA-3' (reverse) for Cx40, 5'-CAAGCTGTGGATCCCGGATACC-3' (forward) and 5'-CTGTCCTGCATTGCTGCCCA-3' (reverse) for Cx40, 5'-GA CCATTGGAACCTCAAAACGAC-3' (forward) and 5'-AGATGTTATCATTCTCAGAGG-3' (reverse) for Cx45, and 5'-GACAGCACTGAC-3' (forward) and 5'-GAGCAGAGCCATGATC-3' (reverse) for β-actin.

**Chemicals**

Buffer chemicals, acetylcholine, and phenylephrine were obtained from Sigma-Aldrich Chemical (St. Louis, MO). U-46619 was purchased from Calbiochem (La Jolla, CA).

**RESULTS**

The arterial pressure of age-matched hamsters (26 wk old) was 108 ± 6 and 165 ± 5 mmHg in the normotensive (CHF-148) and hypertensive (CHF-H4) strains, respectively.

**Characterization of Global Feed Artery Reactivity**

Initial experiments characterized the responsiveness of retractor muscle feed arteries to intravascular pressure and to global application of vasoactive agonists. At 60 mmHg, ∼20% of feed arteries (normotensive and hypertensive strains) displayed >30 μm of myogenic tone. In this subset of vessels, myogenic tone was similar between the two hamster strains as assessed at 60 and 90 mmHg (Fig. 2A). Further experiments using the other 80% of feed arteries, with myogenic tone 22–30 μm, revealed that overall vessel reactivity to superfused vasoconstrictors (phenylephrine or U-46619) did not vary among the two groups of animals (Fig. 2, B and C). Similarly, feed arteries from normotensive and hypertensive hamsters preconstricted with intravascular pressure (60 mmHg) and phenylephrine (3 x 10^{-7} M) dilated in a comparable manner to the global application of acetylcholine, an endothelium-dependent vasodilator (Fig. 2D).

**Conduction of Smooth Muscle-Dependent Responses**

To examine the effects of hypertension on the conduction of smooth muscle-dependent responses, vasoactive agents known to depolarize vascular smooth muscle (41, 42) were discretely applied to a small proportion of a feed artery while vasoconstrictor responses were monitored at sites distal to the point of agent application (Fig. 1). Micropipette application of phenylephrine and KCl initiated a pronounced vasoconstriction at the local application site that conducted poorly along the arterial wall (Fig. 3). Similar to the normotensive controls, smooth muscle-dependent responses conducted poorly along feed arteries from hypertensive hamsters.

**Conduction of Endothelium-Dependent Responses**

The effects of hypertension on the conduction of endothelium-dependent responses were examined by application of acetylcholine to a small proportion of a feed artery while vasodilatory responses were monitored at sites along the vessel wall (Fig. 1). To preconstrict feed arteries, intravascular pressure was first increased to 60 mmHg. Vessels displaying >30 μm of myogenic tone (∼20% of all feed arteries) were identified and studied together. Tone in the remaining vessels was enhanced by addition of phenylephrine (3 x 10^{-7} M) or U-46619 (3 x 10^{-9} M) to the superfusate. In feed arteries isolated from normotensive hamsters and preconstricted with intravascular pressure (60 or 90 mmHg), micropipette application of acetylcholine initiated a vasodilation that conducted with little decay along the vessel wall (Fig. 4). Compared with the normotensive controls, conducted vasodilation in feed arteries from hypertensive hamsters displayed some attenuation, although the trend was not significant. When feed arteries...
were preconstricted with intravascular pressure and agonist, vessels from the normotensive hamsters continued to robustly conduct vasodilation (Fig. 5). In striking contrast, conduction of acetylcholine-induced vasodilation was substantively reduced in the hypertensive strain.

**Cx mRNA and Quantitative Real-Time PCR**

To assess whether hypertension altered Cx mRNA expression, this study quantified the relative mRNA levels of Cx37, Cx40, Cx43, and Cx45 in retractor muscle feed arteries. Initially, primer sets to β-actin and specific Cxs were designed and optimized by real-time PCR on brain cDNA over a range of annealing temperatures. Chromatographs from a bioanalyzer (Fig. 6A) revealed the presence of three peaks, including a low- and a high-molecular-weight standard and a single amplicon generated by each primer set (annealing temperature of 55.1°C). This high reaction specificity was confirmed by melt-curve analysis (Fig. 6B); DNA sequencing verified product identity. As noted by the bracketed number in Fig. 6A, reaction efficiencies exceeded 95% and did not vary by >4.3% among the five primer sets. The relative mRNA levels of Cx37, Cx40, or Cx45 in retractor muscle feed arteries were not different among the two hamster strains (Fig. 6C). Cx43 was, however, substantially reduced in feed arteries from hypertensive hamsters.

**Control Experiments**

The preceding reduction in cell-to-cell communication could, in theory, arise from a genetic difference in the hamster strains that preexists development of hypertension. To control for this possibility, endothelium-dependent conduction was monitored in younger hamsters before the marked onset of hypertension. At 5–7 wk of age, mean arterial pressure was only 10 mmHg higher in hamsters genetically destined to become hypertensive (CHF-H4) than in normotensive controls (CHF-148; Fig. 7A). At this age, acetylcholine-induced vasodilation conducted robustly along feed arteries (preconstricted with 60 mmHg intravascular pressure and 3 × 10⁻⁷ M phenylephrine) from both hamster strains (Fig. 7B). Real-time PCR measurements revealed no quantitative difference in the relative levels of Cx37, Cx40, Cx43, or Cx45 among the two groups of young hamsters (Fig. 7C).

**DISCUSSION**

This study examined the effects of hypertension on cell-to-cell communication in skeletal muscle resistance arteries. To functionally assess vascular communication, vasoactive agents were applied to a small portion of a retractor muscle feed artery while vasomotor responses were monitored at...
sites distal to agent application. In feed arteries isolated from normotensive hamsters, smooth muscle depolarizing agents (41, 42) elicited a localized constriction that conducted poorly beyond the site of agent application. In contrast, discrete application of acetylcholine, an agent known to hyperpolarize the endothelium (9, 41), elicited a robust dilation that conducted with little decay along resistance arteries. Hypertension did not affect the spread of smooth muscle constrictor responses but did attenuate the conduction of endothelium-dependent vasodilation. The attenuated conduction of endothelium-dependent vasodilation occurred, despite a lack of change in feed artery reactivity to intravascular pressure or to global application of phenylephrine, U-46619, and acetylcholine did not vary among the two hamster strains. This maintenance is of key importance, because these vasoactive stimuli were used in the subsequent examination of cell-to-cell communication. As such, any alteration in vessel reactivity would have compli-

Characterization of the Hypertensive Model

The genetic model of hypertension used in this investigation was initially developed by cross-breeding inbred cardiomyopathic hamsters with an outbred strain of golden Syrian hamsters (35). The hypertensive state spontaneously develops within the first 7–10 wk of birth in response to an elevation of blood renin. In accordance with the observations of Thomas et al. (35), mean arterial blood pressure was ~60 mmHg higher in hypertensive hamsters than in normotensive controls. Despite this increase, foundational experiments revealed that feed artery responsiveness to intravascular pressure and to global application of phenylephrine, U-46619, and acetylcholine did not vary among the two hamster strains. This maintenance is of key importance, because these vasoactive stimuli were used in the subsequent examination of cell-to-cell communication. As such, any alteration in vessel reactivity would have compli-
The conduction of endothelium-dependent vasodilation in skeletal muscle arterioles is attenuated by hypertension. In contrast, acetylcholine, a neurotransmitter that reproducibly depolarizes vascular smooth muscle cells, such as phenylephrine and elevated KCl, elicited a localized constriction that failed to robustly conduct along the feed artery wall (33). In contrast, acetylcholine, a neurotransmitter that reproducibly hyperpolarizes the endothelium, elicited a vasodilatory response that conducted with little decay. This differential ability of endothelial or smooth muscle responses to conduct along skeletal muscle arterioles has been previously noted and is a source of active inquiry (17, 33, 43). It has been hypothesized that smooth muscle depolarizing responses poorly conduct because of a flux of Ca\(^{2+}\) into endothelial cells via myoendothelial gap junctions (7, 43). This flux is purported to activate small- and intermediate-conductance Ca\(^{2+}\)-activated K\(^+\) channels and elicit a hyperpolarization that feeds back on smooth muscle to block depolarization (43). Although it is an intriguing hypothesis, others proposed an explanation based on the differential expression of gap junctions between vascular cells (39). In greater detail, past studies have noted that gap junctional expression is far greater between adjacent endothelial cells than between neighboring smooth muscle cells or the two cell layers (10, 12, 20, 21). Such variability would predictably create an environment where the impedance of an endothelial cell would be considerably lower than that of a smooth muscle cell. In such an environment, electrical responses would efficiently spread along the endothelium, but not along the smooth muscle cell layer. Correspondingly, charge movement across myoendothelial gap junctions would be inherently small, and its impact on membrane potential would vary in accordance with cellular impedance. Thus it is logical to reason that a hyperpolarizing response initiated in a small number of endothelial cells should conduct with little decay along this cell layer and elicit a substantive membrane potential response in high-impedance smooth muscle cells. In contrast, a depolarizing response initiated in an equally small number of smooth muscle cells should conduct poorly along this cell layer and elicit only a minimal electrical response in low-impedance endothelial cells.

**Hypertension and Cell-to-Cell Communication**

Past studies employing biochemical approaches and knockout strategies have raised the possibility that disease states such as hypertension could limit cell-to-cell communication in resistance arteries (5, 6, 11). In support of this hypothesis, we report that the conduction of endothelium-dependent vasodila-
tion was attenuated in feed arteries isolated from hypertensive hamsters. Mechanistically, the most plausible explanation for this attenuation is an elevation in coupling resistance between adjacent endothelial cells or between the smooth muscle and endothelial cell layers. For the hypertensive state to enhance coupling resistance, this disease state would have to 1) alter the number or heteromeric composition of expressed gap junctions or 2) reduce their intrinsic activity through second-messenger regulation. Although the small size of hamster retractor muscle feed arteries precludes the quantification of Cx protein, real-time PCR did reveal that the mRNA expression of Cx43 decreased by ~50% in feed arteries from hypertensive hamsters. This reduction in Cx43 mRNA likely occurred in endothelial cells, because work with retractor muscle feed arteries showed that Cx43 is exclusively expressed in this cell layer (28). We speculate that this reduction, if reflected at the protein level, could subtly change coupling resistance. In addition to the downregulation of Cx43, the hypertensive state could have facilitated a rise in coupling resistance by limiting the intrinsic activity of the existing gap junctions. In theory, such reductions in activity could be mediated by PKC and/or mitogen-activated protein kinase (MAPK) (3, 19, 37). Past studies have shown that both phosphotransferases are upregulated in the hypertensive state (23, 36). If these signaling proteins are indeed enhanced in feed arteries from hypertensive hamsters, it is reasonable to assume that their most observable impact on cell-to-cell communication would occur under experimental conditions that ensure their robust activation. Ideal experimental conditions would likely involve the use of vasoconstrictor agonists, including phenylephrine or U-46619, which, through receptor-mediated signaling, can activate PKC and MAPK (2, 4, 29, 44). Such a rationalization may explain why hypertension-induced reductions in cell-to-cell communication were more prominent in feed arteries preconstricted with a combination of intravascular pressure and agonist than in those preconstricted intravascular pressure alone.

Two important issues need to be considered with respect to the preceding argument. 1) One could suggest that the observed reduction in cell-to-cell communication arises from an expressed genetic difference in the animal strains that preexists...
the initiation or development of hypertension. Although this is plausible, control experiments performed on younger hamsters (5–7 wk of age) genetically destined to remain normotensive (CHF-148, n = 4) or to become hypertensive (CHF-H4, n = 4). A: mean arterial pressure of lightly anesthetized CHF-148 and CHF-H4 hamsters. B: diameter response of feed arteries isolated from young CHF-148 (54 ± 6 and 111 ± 9 μm resting preconstricted and maximal diameters, respectively) or CHF-H4 (57 ± 1 and 115 ± 4 μm resting preconstricted and maximal diameters, respectively) hamsters to micropipette application of acetylcholine. Feed arteries were preconstricted with a combination of intravascular pressure (60 mmHg) and 3 × 10⁻⁷ M phenylephrine in the superfusate. Because of their shorter length, cellular conduction could not be measured at the most distal site (i.e., 1,800 μm). C: relative mRNA expression of Cx37, Cx40, Cx43, and Cx45 in feed arteries from CHF-148 and CHF-H4 hamsters.

Functional Implications

Increase in total peripheral resistance is a common feature in animal models of hypertension (15, 25). Past studies have attributed such a change to a broad array of factors, including augmentation of myogenic tone (38), increased sympathetic nerve activity (25), and reduced production of endothelium-derived relaxing factors (15, 16). It could be argued that the attenuation in cell-to-cell communication documented in this study also contributes to this rise in peripheral resistivity. We based this view on the fact that, in peripheral tissue, as in skeletal muscle, vasodilatory signals are often produced within localized regions (32). For such signals to substantively increase tissue blood flow, they would, similar to our experimental pulse of acetylcholine, have to hyperpolarize endothelial cells so as to effectively conduct to regions of the vascular network not exposed to the initial stimulus (9, 32). By diminishing the distance over which endothelial hyperpolarization can conduct, hypertension would shorten the length of vessel controlled by a local vasodilatory stimuli. Consequently, a greater proportion of a given vessel would remain constricted, and this in turn could facilitate a rise in total peripheral resistance.

Final Comments

In summary, the present study demonstrated that hypertension selectively attenuated the conduction of endothelium-dependent vasodilation along retractor muscle feed arteries preconstricted with intravascular pressure and vasoconstrictor agonist. On the basis of these observations, measurements of Cx mRNA, and previously published observations, we propose that hypertension likely attenuates cell-to-cell communication.
REFERENCES


