

White-Coat Effect on Systemic Blood Pressure in Retired Racing Greyhounds

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Background: Greyhounds are known to have a higher systemic arterial blood pressure (BP) than non-Greyhound dogs.

Objectives: The purpose of this study was to determine whether the high systemic BP was because of the white-coat effect.

Animals: Twenty-two healthy retired racing Greyhounds (RRG) enrolled in a blood donation program.

Materials/Methods: We prospectively measured systemic BP in 3 environments: in the hospital by the investigator (Hosp), in the home by the investigator (H/I), and in the home by the owner (H/O). Five serial measurements of systolic, diastolic, and mean arterial pressures (SAP, DAP, MAP) as well as heart rate (HR) were measured by an oscillometric method on the distal forelimb and distal hind limb in all 3 environments.

Results: There was a significant difference for SAP, MAP, and HR between the Hosp and both H/I and H/O ($P < .001$); there were no significant differences for any of the parameters between the H/I and H/O environments. HR, but not SAP, MAP, or DAP ($P < .05$) decreased in RRG with multiple hospital visits for blood donation before this study. The hind limb SAP was significantly higher than the forelimb SAP ($P < .05$).

Conclusions and Clinical Importance: We conclude that the high SAP, MAP, and HR seen in the hospital setting are likely because of a white-coat effect. Furthermore, consideration should be given to defining the parameters of normal BP in RRG according to the environment in which they are obtained.

Key words: Dog; Hypertension; Oscillometric; Stress.

The adoption of retired racing Greyhounds (RRG) has increased in the past decade, with over 120,000 living in homes as pets.¹ This increasing popularity has precipitated considerable research into the many different cardiovascular features of Greyhounds, including higher hematocrit and blood viscosity,² large left ventricular mass and volume,^{3,4} and high systemic arterial blood pressure (BP).^{2,5} Greyhound BP is reported to be approximately 10–20 mmHg higher than that of mixed breed dogs when measured in the hospital.⁶ Most of these cardiovascular differences are physiologic adaptations, presumed to be advantages for racing. Systemic hypertension, however, can have detrimental effects on the cardiovascular, ocular, neural, and renal systems resulting in reversible or irreversible pathologic changes.

White-coat hypertension is defined as an increased BP in the hospital setting when compared with the subject's usual environment (eg, ambulatory BP). The white-coat effect appears to be because of activation of the sympathetic nervous system secondary to stress and resulting in a transient increase in BP.^{7,8–11} In humans, white-coat hypertension can cause target organ damage (TOD) in the kidneys, eyes, and cardiovascular system.^{7,8,12–14} In cats, the white-coat effect can cause an increase in systolic arterial blood pressure (SAP) of up to 30 mmHg when compared with ambulatory BP.⁹ Cats with experi-

Abbreviations:

BP	blood pressure
DAP	diastolic arterial pressure
H/I	investigator at home
H/O	owner at home
Hosp	in-hospital
HR	heart rate
MAP	mean arterial pressure
OSUVMC	Blood Donor Program at the Transfusion Medicine Service, Veterinary Medical Center, The Ohio State University
RRG	retired racing Greyhounds
SAP	systolic arterial pressure

mentally induced renal insufficiency also have white-coat hypertension of even higher magnitude and for a longer duration,⁹ illustrating that when present in animals with concurrent diseases, white-coat effect can lead to an erroneous diagnosis of hypertension.

In dogs, the most common cause of systemic hypertension is renal disease and, the kidneys bear most of the TOD.⁶ According to the 2007 ACVIM Consensus Statement, SAP of 160–179 mmHg represents a moderate risk of TOD, and a SAP > 180 mmHg represents a high risk of TOD.⁶ Renal autoregulation maintains renal blood flow constant up to a SAP of 180 mmHg to protect the kidney from arterial pressure variation.¹³ Persistent hypertension may cause renal vascular changes that can be identified by the presence of microalbuminuria and proteinuria.^{6,14,15} Previous BP studies in RRG showed in-hospital hypertension (> 160 mmHg) that was sustained after blood donation¹⁶ and after several days in the hospital. Microalbuminuria also was observed in 84% of Greyhounds classified as hypertensive.¹⁷ We hypothesized that clinically healthy RRG would have lower systemic arterial BP at home than in the hospital. We also hypothesized that

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BP would be lower at home when the owner obtained the measurements compared with veterinary medical personnel.

Materials and Methods

Twenty-two RRG (12 males, 10 females) enrolled in the Blood Donor Program at the Transfusion Medicine Service, Veterinary Medical Center, The Ohio State University (OSUVMC) were evaluated. All dogs in the Blood Donor Program were appropriately screened and considered healthy. The median age of the males was 7.5 years (range, 4–9 years) with a median body weight of 33.7 kg (range, 30.8–35.7 kg), and the median age of the females was 5.5 years (range, 4–8 years) with a median body weight of 28.3 kg (range, 25.1–32.7 kg). Six dogs weighed <30 kg (all females). Before measuring BP and heart rate (HR) for this study, the number of prior visits to the OSUVMC for blood donation was recorded.

BP measurements were obtained by an oscillometric device^a and an appropriately sized cuff with a width that measured 40–60% of the circumference of the front and rear limbs.^{6,18} The instrument was set to the large cuff size with a cuff inflation pressure of 200 mmHg. Two cuff sites were chosen, the left distal forelimb site (median artery), just proximal to the carpus, placing the cuff arrow on the medial aspect of the leg, and the left distal hind limb site (cranial tibial artery), just proximal to the tarsus, with the cuff arrow on the cranial aspect of the leg. Before application, the cuff was measured and deemed appropriate for each RRG and each limb. The cuff size remained constant for all environments. All dogs were placed in right lateral recumbency with the cuff at or near the level of the heart. The oscillometric device gave readings for systolic, diastolic, and mean arterial blood pressures (SAP, DAP, and MAP), as well as HR. The investigator obtained a femoral pulse during in-hospital measurements to ensure accuracy of the instrument readings. All values were printed directly from the instrument and the values were manually entered in a spreadsheet.

Measurements were taken in 3 environments: in the hospital by the investigator (C.L.M.), in the home by the same investigator, and in the home by the owner (H/O). For 17 dogs, the cranial tibial artery was used before the median artery, and the remaining 5 dogs were evaluated in the opposite order; the order remained constant in the 3 environments. All measurements were obtained between 7:00 and 11:30 AM to eliminate diurnal variation in BP.

Within 15–20 minutes upon arrival at the OSUVMC, the dogs were taken to the blood bank and placed in right lateral recumbency on a cushioned floor. The cuff was placed once the dog was comfortable. The investigator wore scrub clothing and recorded 5 consecutive measurements of SAP, DAP, MAP, and HR for each cuff site. Motion was defined as limb withdrawal and attempts at standing during the measurement process; associated recordings were discarded. Only 18 of the 22 dogs donated blood after obtaining the measurements. All at-home BP and HR measurements were

made between 7 and 28 days after the hospital measurements to avoid any effects of blood donation.

The same investigator (wearing scrub clothing) arrived at the dog's home. The dog was taken to a known comfortable place in the home, as identified by the owner, and placed in right lateral recumbency. The cuff was placed as described above when the dogs were calm (ie, they lay motionless without restraint) about 5–10 minutes after arrival. Five consecutive readings were obtained while the investigator instructed the owner on how to operate the device. Detailed written instructions also were left with the owner. The owner was provided with a questionnaire to ensure the dog was calm, motionless, and had not recently exercised before their measurements. The owner repeated the BP measurement process described previously 24 hours after the investigator. The questionnaire was returned with the printed values. This study was performed in accordance with The Ohio State University Institutional Animal Care and Use Committee.

By GraphPad Prism software,^b normality was evaluated by the D'Agostino-Pearson method. A one-way repeated-measures analysis of variance was used to compare differences in SAP, DAP, MAP, and HR among the 3 environments: in the hospital (Hosp), in the home by the investigator (H/I), and in the H/O. A *t*-test was used to compare the SAP, DAP, MAP, and HR between the median artery and the cranial tibial artery. A *t*-test was used to compare the values for SAP, DAP, MAP, and HR between males and females, and between dogs weighing <30 kg and >30 kg. A Pearson correlation was used to evaluate the effect of number of blood donations on SAP, DAP, MAP, and HR. A *P*-value of <.05 was considered significant. All values are reported as mean ± SD.

Results

All BP measurement results are presented in Table 1. The Hosp SAP and MAP were significantly higher than both the H/O and H/I SAP and MAP ($P < .001$ and $P < .001$, respectively; Table 1, a, b, e, f; Fig 1); there were no significant differences for SAP and MAP between the H/O and the H/I (Table 1). The Hosp DAP was significantly higher than the H/O DAP ($P = .02$), but not the H/I DAP (Table 1, c and d). The Hosp HR was significantly higher than the H/I and H/O HR ($P < .001$; Table 1, g and h), but there was no significant difference in HR between H/I and H/O. The mean number of donations before this study was 11 (range, 0–32). The HR decreased significantly ($P = .04$) with increasing number of donations; there were no significant differences among SAP, MAP, and DAP and number of donations (Fig 2).

The Hosp SAP was significantly higher when measured using the cranial tibial than when using the median artery ($P = .04$), as were SAP H/I ($P = .004$) and SAP H/O

Table 1. Average SAP, MAP, DAP, and HR in the median and cranial tibial arteries across 3 different environments.

	Median Artery [‡]			Cranial Tibial Artery [‡]		
	Hosp	H/I	H/O	Hosp	H/I	H/O
SAP [‡] (mmHg)	154 ± 17 ^a	133 ± 13 ^a	130 ± 12 ^a	165 ± 17 ^b	147 ± 17 ^b	141 ± 13 ^b
DAP (mmHg)	88 ± 15 ^c	82 ± 15	80 ± 11 ^c	96 ± 14 ^d	86 ± 15	84 ± 14 ^d
MAP (mmHg)	110 ± 14 ^c	98 ± 13 ^c	95 ± 10 ^c	116 ± 14 ^f	104 ± 15 ^f	101 ± 13 ^f
HR (bpm)	111 ± 17 ^g	77 ± 27 ^g	65 ± 26 ^g	116 ± 15 ^h	78 ± 24 ^h	67 ± 21 ^h

Significant difference within same letter.

[‡]Significant difference in parameter between groups.

DAP, diastolic arterial pressure; H/I, investigator at home; H/O, owner at home; Hosp, in-hospital; HR, heart rate; MAP, mean arterial pressure; SAP, systolic arterial pressure.

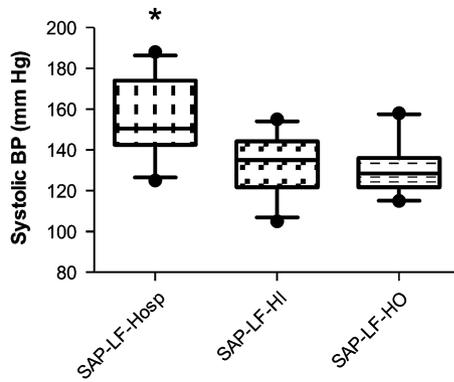


Fig 1. Systolic arterial pressure (SAP) in both legs across 3 environments. Whiskers indicate 5th and 95th percentiles.

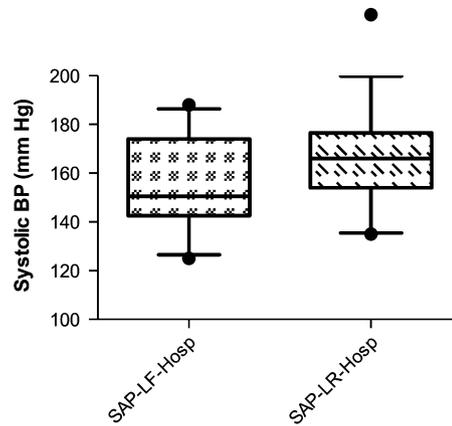


Fig 3. Systolic arterial pressure (SAP) difference from front and back legs. Whiskers indicate 5th and 95th percentiles.

($P = .008$; Table 1; Fig 3). In contrast, DAP, MAP, and HR were not significantly different between the front limb and the rear limb in any of the 3 environments. The Hosp SAP in the median artery (but not in the cranial tibial artery) was significantly higher in males than in females ($P = .02$; data not shown). No significant difference was found in SAP between groups for dogs that weighed < 30 kg or > 30 kg (data not shown).

Discussion

Results of this study demonstrate that RRG do experience white-coat effect on BP in the hospital environment. The mean hind limb SAP in hospital was 165 mmHg, whereas at home it was lower, with or without the investigator's presence, at 131 and 133 mmHg, respectively. MAP, DAP, and HR followed a similar pattern. HR was lowest in RRG that had been acclimated previously to the environment with multiple hospital visits, but, BP did not follow a similar pattern. Although RRG are thought to have higher BP than mongrel dogs, this study emphasizes the need to consider the environment in which the BP is measured before diagnosing or eliminating hypertension, and that normal BP for RRG may be similar to other dogs.

Several cardiovascular features in RRG that differ from those in other dog breeds have been recognized over the past few decades. Most of these features are considered

adaptations to racing because of the increased oxygen reserve required for acceleration and speed. Previous reports documented that RRG have SAP approximately 10–20 mmHg higher than that of the average mixed breed dog.^{2,5,6} Interestingly, SAP in untrained Greyhounds was not different from that in other breeds.^{3,13,6} Also, in a recent study of 48 RRG, mean SAP recorded in the hospital was 161 mmHg, SAP remained constant after 3 days of hospitalization, and half of the dogs were classified as “hypertensive” according to current guidelines.¹⁷ Our results are similar to these previous studies, with a high Hosp mean SAP of 155–165 mmHg, depending on the limb used for cuff placement. However, our study also showed that compared with Hosp measurements, at-home BP (H/I and H/O) was significantly lower, indicating that a white-coat effect on BP occurs in RRG. There also was a significant decrease in HR between the Hosp and at-home measurements, suggesting alterations in sympathetic tone and stress level between environments, and further supporting the occurrence of white-coat effect in the dogs studied.

The low at-home mean SAP of approximately 130 mmHg for the median artery and 140 mmHg for the cranial tibial artery in RRG challenges the concept that RRG have a physiologically higher SAP than other breeds. The white-coat effect has been demonstrated previously in clinically healthy mongrel dogs, by an oscillometric BP technique, with the highest in-hospital SAP of 158 mmHg and the mean in-home SAP of 128 mmHg,¹⁹ pressures similar to those in our study. Interestingly, in our study we found no differences in BP in the home environment when either the investigator or the owner obtained the readings, suggesting that the decrease in stress level and BP may be because of the environment of BP measurement or the owner's presence during the measurement. Additional studies are indicated to determine whether the owner's presence in the hospital decreases white-coat effect in RRG.

In most humans, white-coat effect on BP lasts for a short time and BP returns to normal.²⁰ Cats are similar, with acclimation to the environment in just 10 minute. When the cat is moved or handled again, the white-coat effect diminishes more quickly each time during that office visit.⁹ A study using clinically healthy Beagles also showed a decrease in BP over 3 weeks after acclimation

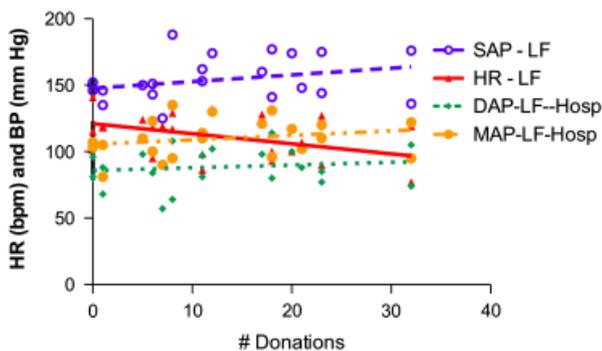


Fig 2. Relationship among heart rate (HR), systolic, mean, and diastolic arterial pressures (SAP, MAP, and DAP) with prior number of blood donations. There was a significant decrease in HR with increased number of donations ($P = .04$).

to the environment and procedures.²¹ Although not all dogs acclimate to the hospital, many studies indicate the majority of dogs do adapt over time.^{6,19,21} Thus, the standard for measuring BP is to wait 8–10 minutes once the animal is in the hospital to allow for acclimation to occur. RRG do not appear to experience this acclimation, and maintain higher SAP over the course of hours to days.^{16,17} This finding is supported by our study where there was no significant difference in the hospital SAP between those RRG that had donated blood multiple times before this study (ie, “veteran donors” acclimated to the blood bank) and those that had never donated before. This feature of RRG can make it difficult to distinguish true hypertension from white-coat hypertension in the hospital setting, regardless of their familiarity with surroundings and procedures.

HR is an indicator of stress and anxiety in humans.²⁰ As discussed above, HR was significantly higher in the hospital than in the home environment, likely because of a stress response and increased sympathetic nervous system activation. However, HR in RRG were significantly lower in the “veteran donors.” The familiarity of surroundings and routine may eliminate some stress, but unexpectedly, SAP, MAP, and DAP were not different in the “veteran donors.” The reason for this finding is unclear, but may be because of humoral or local vasomotor factors contributing to a persistent increase in systemic vascular resistance despite decreased sympathetic activation. These findings are additional evidence supporting a lack of BP acclimation and an indication that HR measurement may not be an accurate indication of stress level and white-coat effect in RRG.

White-coat hypertension in humans is associated with an increased risk for subsequently developing hypertension and TOD.²² High SAP, or hypertension, can cause vascular changes in the kidney leading to microalbuminuria, proteinuria, and an increased risk for developing renal disease. We have observed that protein-losing nephropathy (PLN) because of glomerulonephritis is common in RRG (data not shown). Possible explanation for the high prevalence of PLN is that RRG have sustained high SAP, and thus mimic humans with hypertension-induced renal disease. Interestingly, in another study¹⁷ most of the “hypertensive” Greyhounds had microalbuminuria, whereas the “normotensive” ones did not. Whether white-coat hypertension causes TOD in dogs is unclear and requires additional study.

Oscillometric SAP and MAP appear to correlate with direct arterial pressure with a difference <10 mmHg.²³ However, other studies indicate that both Doppler and oscillometric methods underestimate SAP, DAP, and MAP in laterally recumbent dogs, with SAP having a greater difference from direct measurements than DAP and MAP.^{6,24} In Sighthounds, indirect SAP tended to show an even greater difference from direct pressures, but correlations with direct pressure improved with serial measurements.²⁴ DAP has the highest variation and weakest correlation with direct pressures at all cuff sites,²⁴ which may explain the lack of difference between the in-hospital DAP and the at-home DAP (obtained by the investigator). This finding also may represent a type II error, and a larger sample size may have shown a sig-

nificant difference in DAP across all 3 environments. Finally, some studies indicate that all Doppler measurements correlate better with direct pressures than oscillometric measurements,²⁴ whereas others show both Doppler and oscillometric SAP have similar correlations with oscillometric MAP correlating best.²³ Oscillometric measurements were used in this study because of the ease of having owners measure BP at home.

A study that included Sighthounds found the closest correlation with direct pressures for all measurements with the cuff on the median artery, followed by the coccygeal artery, but the correlation of direct with indirect pressures of the cranial tibial artery also was significant.²⁴ Another study using Beagles showed the best correlation with the cranial tibial artery and the coccygeal artery.²⁵ Using the distal forelimb site just proximal to the carpus (median artery) and the distal hind limb site just proximal to the tarsus (cranial tibial artery) in this study, the cuff size remained constant across all measurements. We found SAP measured at the cranial tibial artery to be significantly higher than that measured at the median artery, which was assumed to be related to acclimation because the hind limb was measured before the forelimb. However, when the order of readings was reversed with the remaining 5 dogs, the hind limb SAP remained higher (data not shown). Interestingly, a study in mongrel dogs showed BP measured from the metatarsus was significantly higher than BP measured from the metacarpus in the hospital and home environments similar to our findings, but, the decrease was attributed to acclimation which did not occur in our study.¹⁹ After selecting cuff size based upon previously stated criteria for this study, the same cuff size was used for the forelimb and hind limb, and the hind limbs were measured to be slightly larger (3–4 mm) than the forelimbs (data not shown). SAP measured in the forelimb may have been lower because of the slightly larger circumference to cuff ratio than the hind limb, but it is unlikely this small difference in size would have an important effect. The difference between limb BP measurements might also be because of the vascular conformation of Greyhounds and their higher oxygen demand in the hind limbs for racing, or a different anatomical conformation of the hind limb musculature that alters the oscillometric reading when compared with the forelimb. The reason for the increased hind limb SAP could not be determined from this study.

The limitations of this study include the inability to obtain paired direct and indirect arterial pressures in all environments, the inability to monitor and assess the owner’s competency in performing the procedure, and the lack of environmental randomization. Direct arterial pressures would not have been possible in the home environment, with or without the investigator, and would have been much more invasive and technically difficult in the hospital. The reason for the increased hind limb SAP is unclear, but without direct arterial pressures it is difficult to determine whether the difference was caused by instrument error because of muscle conformation or cuff size, or if SAP actually is increased in the hind limb in RRG. Although monitoring was not possible, the owners

witnessed the procedure and were left with detailed instructions and a questionnaire to perform on their own. The owner readings were similar to the investigator readings in the home environment, leading us to believe the procedure was followed appropriately. Finally, the BP measurements in the 3 environments were not completed in a random order, suggesting the decrease in BP from the hospital to the home environment could be because of procedural acclimation. A final BP reading in the hospital would discredit this suggestion of acclimation. It is known, however, that RRG do not acclimate to the procedure across hours after blood donation with the fourth measurement similar to the first, or across days in the hospital with 2 separate measurements.^{16,17} Additionally, in a study using Beagles, each time BP was measured over the course of 135 days, a decrease occurred, with the greatest decrease during the first 4 measurements.²¹ Therefore, with procedural acclimation one would expect BP measured in the home environment without the investigator to have been lower than that measured with the investigator present. Although a final BP was not taken in hospital, it is likely that the RRG BP would be increased similar to their first BP experience.

In conclusion, when attempting to differentiate true systemic hypertension from white-coat hypertension in RRG, acclimation to the environment does not appear to be sufficient. Rather, the BP should be measured in the home environment, keeping in mind that the hind limb cuff site will result in higher SAP readings. Additionally, we propose that RRG may have similar BP to other dogs, but that when measured in the clinic, white-coat effect results in a falsely increased reading. Future studies are needed to determine whether white-coat hypertension leads to clinically relevant TOD (eg, microalbuminuria and renal disease) in RRG.

Footnotes

^a Cardell, model 9402; Sharn Veterinary Inc, Tampa, FL

^b Gradpad Prism v.4, GraphPad Software Inc, San Diego, CA

Acknowledgments

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