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Associations Between Canine Juvenile Weight Gain and Coxofemoral Joint Laxity at 16 Weeks of Age

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Abstract

Objective—Evaluation of the relationship between canine weight gain from 6 to 15 weeks of age and passive coxofemoral joint (CFJ) laxity at 16 weeks of age.

Study Design—Longitudinal cohort study.

Animals—Full- or half-sibling hounds ($n = 56$).

Methods—Hounds were weighed weekly from 6 to 15 weeks of age. Individual average daily gain (ADG) was calculated for each week (weekly) and for the study (overall). PennHIP distraction index (DI) was determined for each CFJ at 16 weeks. Mixed effects linear models were evaluated for associations of DI (highest and mean) with 15-week weight and ADGs (actual or normalized). Left and right DIs were compared with a Student's paired t-test. Significance was set at $P < .05$. Trends were considered at $P < .10$.

Results—Mean ($\pm$ SD) 16-week DI score and 15-week weight was 0.67 ± 0.16 and 12.5 ± 1.8 kg, respectively. Within animal left and right DIs were not significantly different. There were no significant associations between DI and any of the weight gains evaluated. There was a trend for a negative relationship between normalized 14-week ADG and DI in one statistical model.

Conclusions—Weight gain from 6 to 15 weeks of age was unrelated to 16-week PennHIP DI in a homogenous canine population with moderate-to-severe CFJ joint laxity.

Clinical Relevance—Based on our results, ad libitum feeding between 6 and 15 weeks of age does not appear to have an adverse impact on joint laxity at 16 weeks of age as measured by the PennHIP DI.

INTRODUCTION

The precise pathophysiology underlying the transformation of apparently normal neonatal canine coxofemoral joints (CFJs) into malformed, osteoarthritic adult CFJs has been a focus of research since canine hip dysplasia (CHD) was identified by Schnelle over 40 years ago.¹ The condition is difficult to eliminate because of its multifactorial polygenic nature.^{2–5} Heritability varies widely, depending on breed and cohort, with reported heritability scores as high as 0.6 and as low as 0.11.^{6,7} A heritability score of 1.0 coincides with complete

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genetic control of disease expression whereas a score of 0.0 indicates complete lack of genetic contribution, so, based on CHD heritability scores, environmental influences are often vital to development of the CHD phenotype. Elucidations of the impact of specific environmental factors on CHD expressivity contribute to further understanding of CHD pathophysiology.

The contribution of nutritionally dependent early, rapid growth, and weight gain to CHD severity has garnered substantial attention beginning as early as 1964.^{8–14} Dogs with the highest growth rate experience early, and ultimately severe, effects of CHD.¹⁵ The first susceptible period appears to be from 3 to 8 months of age, though the first 6 months are reportedly most critical.^{7,15} Investigations of the relationship between weight gain and CHD have varied widely in duration, nutritional variables, and study populations, but to our knowledge, none have focused entirely on the immediate post-weaning period.^{8–11,13–16} Specific evaluation of this stage may provide further insight on the relationship between weight gain and the CHD phenotype.

CFJ laxity is an established component of CHD, though its exact role has not been completely defined.^{10,17} It is assumed to contribute to the initiation and progression of CFJ osteoarthritis (OA) characteristic of CHD as a result of trauma to, and abnormal wear on, the articular structures.^{7,18} Passive CFJ laxity, quantified by the PennHIP distraction index (DI), in puppies as young as 16 weeks of age is associated with development of adult CFJ OA.¹⁷ Events leading to pathologic CFJ changes characteristic of CHD, including abnormal joint laxity, are reported to begin in the early neonatal period.¹⁹ Evidence to support heritability of joint laxity has been reported, though a mode of inheritance has not been fully described.²⁰ Kealy et al¹⁰ documented an association between weight gain and CFJ laxity in Labrador Retrievers as early as 30 weeks of age. Kasström et al⁹ found a closer relationship between ultimate CHD severity and weight gain than with CFJ laxity determined before 12 weeks of age. Given the relationships between both juvenile weight gain and CFJ laxity with adult CHD, it is possible that early weight gain may affect passive CFJ laxity contributing to CHD. This study was specifically designed to investigate the relationship between weight gain in the immediate post-weaning period and passive CFJ laxity at 16 weeks of age in a population of puppies predisposed to develop CHD. We hypothesized that CFJ laxity would be greater in puppies with the highest rates of weight gain between 6 and 15 weeks of age.

MATERIALS AND METHODS

Dogs and Housing

A total of 56 mixed-breed hounds from 9 separate litters were selected for this study. There were 23 males and 33 females. The hounds were the progeny of 6 dams (22–27 kg) and a single sire (30 kg). Members of the parental generation were unrelated individuals from a closed hound colony. Moderate-to-severe CFJ disease was apparent on PennHIP radiographs of all dams, and the sire was severely affected. DIs could not be determined for any of the parents because of the presence of pathologic joint changes. Litters were delivered vaginally, kept with their dams until weaning at 6 weeks of age, and then housed together in 3 m × 4 m indoor rooms with concrete floors for the duration of the study. The study was not initiated until weaning to exclude potential differences resulting from inherent variability of maternally derived nutrition. Exercise was not controlled for purposes of this study.

Diet—PMI Nutrition Prime Formula (PMI Nutrition, Henderson, CO) was fed to dams during gestation and lactation and ad libitum to puppies after weaning. The manufacturer's guaranteed analysis included a minimum of 26% crude protein, 18% crude fat, 3.5% crude fiber, 1% calcium, 0.8% phosphorus, 1.6% linoleic acid, 10,000 IU/kg vitamin A, and a

maximum of 12% moisture with 4.02 kcal/g digestible calories. This food preparation meets the Association of American Feed Control Officials requirements for canine growth. Depending on litter size, food was provided in 1–4 feeders/run to limit competition, and fresh kibble was provided twice daily. Quantities of kibble, fed to puppies, were increased as necessary to ensure that food remnants remained in the bowls when they were replaced with fresh kibble in clean bowls twice daily. Water was available ad libitum throughout the study.

Body Weight

The weight (kg) of each puppy was obtained on the same day of each week from 6 to 15 weeks of age. Average daily gain (ADG) was calculated for each week and over the period from 6 to 15 weeks of age. Specifically, the current week's weight was subtracted from the previous week's, and divided by 7 to yield the ADG for the week (weekly ADG). To determine the ADG for the study (overall ADG), the initial weight at 6 weeks of age was subtracted from the final weight and divided by 63. All ADGs were normalized by dividing each by the weight at the earliest week in the observation and multiplying by 100 as follows: $[(\text{week}_2 \text{ weight} - \text{week}_1 \text{ weight})/7]/\text{week}_1 \text{ weight} \times 100$. Overall ADG was normalized to the initial weight similarly.

Radiographic Evaluation

All puppies had a complete physical examination before radiographic evaluation. Each puppy was anesthetized and PennHIP CFJ radiographs were obtained at 16 weeks of age using established techniques.²¹ All radiographs were performed by a PennHIP licensed individual (J.B.). DI for each CFJ was determined by PennHIP personnel (PennHIP, Malvern, PA). DI was considered to be an objective measure of passive CFJ laxity for this study.^{17,18,22} For analysis purposes, the highest and mean DI of each dog were determined.

Statistical Analysis

Descriptive statistics were determined for each ADG as well as the 15-week weight. Left and right DIs were compared with Student's t-test for paired observations. Mixed effects linear models were evaluated for associations of DI (highest or mean) with sex, week 15 weights and each ADG as fixed effects; litter was included as a random effect. Separate models were evaluated for ADG and normalized ADG with all weeks and 15-week weight included. To reduce the potential for multicollinearity among regressors, similar models were evaluated with only weeks 6–7, 10–11, and 14–15 ADGs included. All statistical tests were performed with a commercially available software program (SAS v9.1, SAS Institute Inc., Cary, NC), and significance was set at $P < .05$. Trends were considered at $P < .10$.

RESULTS

All puppies remained healthy, were in good body condition, and maintained normal activity levels. Physical examination findings were within normal limits at 16 weeks of age. Mean ($\pm$ SD) litter size was 6 ± 2 (range, 2–8 puppies). Mean CFJ DI score was 0.67 ± 0.16 (range, 0.38–1.05) and there was no radiographic evidence of OA in any CFJ. The 15-week weight was 12.5 ± 1.8 kg (range, 8–17 kg). ADG was most variable between individuals in the 7 to 8 week interval and least variable in the 11–12-week interval (Table 1). Left and right DIs were not significantly different within animals ($P = .07$). There were no significant litter or gender effects in any mixed effects linear models. Highest or mean DI was not significantly correlated with any ADGs in models including all ADGs (weekly or overall; actual or normalized) and 15-week weight. In models with only weeks 6, 10, and 14 ADGs and 15-week weight included, there were trends for negative correlations between both highest ($t = -2.03$; $P = .06$) and mean ($t = -2.01$; $P = .06$) DI normalized week 14–15 ADG (Fig 1).

DISCUSSION

Based on our findings, we rejected our hypothesis that CFJ laxity would be greater in puppies with the highest rates of weight gain between 6 and 15 weeks of age in a CHD predisposed population. Study subjects were selected based on the likelihood that they would develop CHD. The probability of developing CFJ OA characteristic of CHD increases somewhat proportionately with DI scores ≥ 0.30 .²³ With a mean DI score of 0.67 in the study population, most puppies were prone to CFJ changes consistent with CHD. Puppies were radiographed for DI determination at the youngest age that scores are reported to be prognostic, though this varies between breeds.^{18,24} Whereas DI scores from radiographs performed later may have been more prognostic for CHD, this was not feasible in this study. We quantified CFJ laxity by PennHIP DI an objective, measurable variable that is strongly associated with the CHD phenotype at maturity. However, no conclusions are stated or implied as to the adult CHD status of the study subjects.

The lack of association between passive CFJ laxity and weight gain we found contrasts with most of the available literature, which suggests a beneficial effect of decreased weight gain mediated by caloric restriction on both CHD expression and CFJ laxity.^{7,9,10,13-15,25} These apparent differences may be explained by study dissimilarities. To our knowledge, this is the first investigation to assess associations between passive CFJ laxity quantified by PennHIP DI and weight gain. Whereas radiographic methods of passive laxity determination may be relatively comparable, the methods and interpretations are not identical.^{22,23} Additionally, we assessed weight gain weekly in the immediate post-weaning period whereas most other investigations were longer in duration with greater intervals between weight gain determinations.⁸⁻¹⁴ The CHD phenotype is highly variable in a number of ways including progression rate and ultimate severity.^{5,26-28} It is possible that some of the variability results from specific breed differences in the disease.^{3,24,29,30} Our hounds may be affected by a familial form of CHD similar to a variety of human developmental hip dysplasia³¹ because all puppies had the same sire. This fact alone could explain differences between study findings.

Ours was an observational study so treatment groups characteristic of interventional studies were not included in the design. To best observe relationships between DI and weight gain, multiple steps were taken to limit potential environment and genetic variability. The growth rate of our puppies was likely maximal or submaximal as found previously in ad libitum fed puppies, though we did not validate this by body composition determinations;⁹ however, all puppies were perceived to be in good body condition when examined by a licensed veterinarian at 16 weeks of age. Whereas steps were taken to limit food competition between puppies, inherent personality differences could have influenced feed intake, contributing to the weight gain ranges we observed. Additionally, there was a wide range of puppy sizes, so weight gain was normalized. This may be the first study of its kind to include a canine population sired by a single individual, potentially reducing individual differences caused by breed and genetic variation.³² Litter and gender effects were considered in each statistical evaluation, and a model was designed to reduce the potential effect of co-linearity caused by close chronologic sampling proximity. Associations between weight gain and CFJ laxity might vary between growth phases and the trends for negative correlations with normalized 14-15-week weight gain may be indicative of impending associations.^{9,13,16}

Based on our preliminary findings, weight gain from 6 to 15 weeks of age is unrelated to 16-week PennHIP DI in a homogenous canine population with moderate-to-severe CFJ laxity. It is possible that ad libitum feeding during this period of growth does not have an adverse impact on joint laxity at 16 weeks of age. Further studies are necessary to unequivocally

confirm this possibility. Our results emphasize the need for further identification and elucidation of environmental influences on the CHD phenotype.

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Appendix

PMI Nutrition® Prime Formula List of Ingredients

Meat and bone meal, ground yellow corn, brewers rice, animal fat (preserved with BHA and citric acid), corn gluten meal, chicken by-product meal, ground wheat, natural poultry flavor, beet pulp, sunflower oil, salt, potassium chloride, fish meal, dried whey, choline chloride, ferrous sulfate, zinc oxide, vitamin E supplement, niacin, copper sulfate, manganous oxide, vitamin A supplement, calcium pantothenate, biotin, vitamin B12 supplement, pyridoxine hydrochloride, thiamine mononitrate, menadione sodium bisulfate complex, calcium iodate, vitamin D3 supplement, riboflavin supplement, cobalt carbonate, folic acid, sodium selenite.

Fig 1. Linear regression of normalized weeks 14–15 average daily gain (ADG) to highest (▲) and mean (■) distraction index (DI) score for each puppy.

Table 1

Actual and Normalized Average Daily Gain (ADG) of Hound Puppies Fed Ad Libitum for Each Weekly Interval and over the Study Period

Weeks	ADG $\pm$ SD; Range (kg)	Normalized ADG $\pm$ SD; Range
6–7	0.22 $\pm$ 0.24; 0.00–0.79	3.30 $\pm$ 1.37; 0.00–6.48
7–8	0.22 $\pm$ 0.28; 0.01–1.03	2.94 $\pm$ 1.77; 0.25–8.89
8–9	0.15 $\pm$ 0.07; 0.01–0.36	2.71 $\pm$ 1.53; 0.28–8.93
9–10	0.17 $\pm$ 0.07; 0.00–0.39	2.63 $\pm$ 1.27; 0.06–7.76
10–11	0.15 $\pm$ 0.06; 0.00–0.37	1.93 $\pm$ 0.83; 0.00–4.82
11–12	0.12 $\pm$ 0.06; –0.07–0.33	1.36 $\pm$ 0.70; –0.73–3.61
12–13	0.13 $\pm$ 0.06; 0.02–0.26	1.29 $\pm$ 0.60; 0.15–3.22
13–14	0.13 $\pm$ 0.08; –0.06–0.31	1.20 $\pm$ 0.76; –0.54–2.64
14–15	0.16 $\pm$ 0.17; 0.00–0.41	1.45 $\pm$ 0.83; 0.00–3.59
6–15	0.15 $\pm$ 0.03; 0.08–0.22	3.71 $\pm$ 0.89; 1.63–5.38