

## ORIGINAL RESEARCH

# Temporal changes in the presence and intensity of innocent cardiac murmurs in clinically healthy Cairn terrier and Dachshund puppies between 4 and 8 weeks of age

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**Abstract**

**Background:** Spontaneous week-to-week variation in the presence and intensity of innocent cardiac murmurs in individual puppies is unknown.

**Methods:** Sixty privately owned, clinically healthy Cairn terrier and Dachshund puppies between 4 and 8 weeks of age were included. All dogs underwent weekly cardiac auscultation at the breeders' home by a veterinary cardiology specialist using an acoustic stethoscope. On each occasion, a phonocardiogram was recorded with an electronic stethoscope. Furthermore, all dogs were auscultated once at a first opinion veterinary practise and once at the authors' institution, where they also underwent an echocardiographic examination.

**Results:** Two-hundred and eighty-one auscultations were conducted on 32 Cairn terriers and 28 Dachshunds, at the breeders' homes. Innocent murmurs were detected in 19 puppies. Two of these puppies had a detectable murmur on each auscultation. In five of the puppies, the murmur became undetectable during the observation period and in 12 puppies the murmur was intermittently audible. Auscultation at the authors' institution had an unpredictable effect on murmur presence and intensity. Phonocardiography revealed murmurs in 42 puppies. Interpretation of phonocardiograms by two independent observers showed nearly perfect agreement ( $\kappa = 0.859$ ).

**Conclusions:** Remarkable and unpredictable spontaneous week-to-week variation was documented in the presence and intensity of innocent murmurs.

**KEYWORDS**

auscultation, inter-observer agreement, phonocardiography, screening

**INTRODUCTION**

Innocent cardiac murmurs are common findings in clinically healthy puppies that are presented to first opinion veterinary practices for health checks at 6–7 weeks of age.<sup>1</sup> Contrary to most pathological murmurs, innocent murmurs tend to be soft, localized in the left heart base, limited to early systole, and become undetectable spontaneously as the puppy ages.<sup>2–4</sup> A recent study showed a marked difference in the prevalence of soft systolic murmurs in clinically healthy puppies when they were assessed by first opinion veterinary practitioners and, on aver-

age, 9 days later by a veterinary cardiology specialist.<sup>5</sup> The factors responsible for this discrepancy remained unclear.

The aims of this prospective study were to determine whether, in clinically healthy puppies between 4 and 8 weeks of age, (1) there is a spontaneous week-to-week variation in the presence and intensity of innocent cardiac murmurs, (2) stress caused by a different environment (i.e., breeder's home vs. the veterinarian's consultation room) has an effect on the presence and intensity of innocent murmurs, (3) the auscultation findings of first opinion veterinary practitioners differ from those of a veterinary cardiology specialist,

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(4) there is a correlation between the auscultation findings of a veterinary cardiology specialist as collected with an acoustic stethoscope compared to phonocardiograms recorded with an electronic stethoscope by the same investigator and whether (5) there is a high level of agreement in the interpretation of the recorded phonocardiograms between two independent investigators.

## MATERIALS AND METHODS

In this prospective, longitudinal and observational, cohort study, all owners signed an informed consent form and participated in the study on a voluntary basis. All animals were handled according to institutional ethical guidelines.

### Animals

Privately owned, clinically healthy Cairn terrier and Dachshund puppies were recruited through various breeders between September 2017 and July 2018. The individual puppies were initially identified by colour-coded collars and later by their microchip (transponder) registration numbers. All dogs were clinically healthy based on the history taken from the breeders and on the physical examination performed by the veterinary cardiology specialist (Viktor Szatmári) participating in this study.

### Auscultation

As of 4 weeks of age, each puppy was auscultated once a week at the breeder's home by a single veterinary cardiology specialist using an acoustic stethoscope with a diaphragm size of 30 mm. For each examination, each puppy was examined while standing on a table. After the first examination, all puppies were subsequently re-examined weekly under the same environmental, positioning and handling conditions until they were sold to a new owner. Once a murmur was detected, the following variables were noted: timing (systolic, diastolic or continuous), the point of maximal intensity (left or right heart base or apex) and intensity (scale 1–6), as well as other characteristics, such as beat-to-beat variability in intensity, and musical character.<sup>1–5</sup> Special attention was also made to auscultating the left axilla to detect potential left-to-right shunting patent ductus arteriosus.

Immediately after auscultation with an acoustic stethoscope, the cardiac auscultation was repeated with an electronic stethoscope (3M Littmann Electronic Stethoscope Model 4100WS; 3M Health Care, MN, USA) with a diaphragm size of 50 mm. Auscultation was performed at the point of maximal intensity of the murmur, or at the left heart base in puppies where no murmur was detected. Using this electronic stethoscope, a digital phonocardiogram was recorded and stored.

In addition to auscultations at the breeders' homes, each puppy underwent one cardiac auscultation at the authors' institution. This auscultation was immediately followed by an echocardiographic examination performed by the same veterinary cardiology specialist who auscultated the dog on the echocardiography table at the authors' institution.

Additionally, during the course of the study, each puppy underwent one cardiac auscultation at the time of first vaccination by a first opinion veterinary practitioner from one of the various participating veterinary practices. The auscultation findings of the first opinion veterinary practitioners were recorded on the health certificate page of the pets' health passports.

Auscultation findings from the veterinary cardiology specialist's evaluations were tracked longitudinally and compared to previous findings for each puppy. The specialist's auscultation findings from the authors' institution and the closest evaluation (in time) performed at the breeder's home were also compared. Depending on the situation, auscultation at the breeder's facility could take place before or after the evaluation of the puppy at the institution. Last, auscultation findings from the veterinary cardiology specialist were compared to those of the first opinion veterinary practitioner. For this last comparison, findings of the first opinion veterinary practitioner were compared to the findings of the veterinary cardiology specialist that took place at the closest (in time) breeder's home visit, as well as to auscultation findings from the evaluation of the puppies at the authors' institution.

### Phonocardiography

The phonocardiograms were analysed on a computer screen using the software of the electronic stethoscope (3M Littman Sound Analysis software Version 2.0.c. for heart sounds; 3M Health Care). The digital filter was set on Diaphragm Mode, and the speed varied between 25–100 mm/s. The median duration of the recordings was 8 s (range: 3–8 s). The phonocardiograms were reviewed by two authors (Donny Rigterink and Mariska A. L'Herminez) for visible indications of a heart murmur according to published guidelines.<sup>3,6</sup> These two authors carried out the interpretation independently from each other with several months' time difference. They were blinded to each other's findings and to the veterinary cardiology specialist's auscultation and echocardiographic findings. If a murmur was visible on phonocardiography at every cardiac cycle, this was scored with a 1, while an intermittently detectable murmur was scored with a 0.5, and the lack of a detectable murmur was scored with a 0. Segments, where murmurs could not be clearly detected due to artefacts, were excluded from the analysis.

Two comparisons were carried out on the phonocardiographic data: (1) the veterinary cardiology specialist's auscultation findings at the breeders' home at each time point were compared to the phonocardiograms recorded on the same day and (2) the phonocardiographic findings of two independent

investigators (Donny Rigterink and Mariska A. L'Herminez) were compared for agreement.

## Echocardiography

To exclude structural (congenital) cardiac diseases as a possible cause of a murmur, all puppies underwent an echocardiographic examination once during the study period by the same investigator who performed the serial cardiac auscultations. All echocardiographic examinations took place at the authors' institution using 2D, colour Doppler and spectral Doppler techniques according to published guidelines.<sup>3,7</sup>

For the Cairn terriers, the echocardiographic examination and the auscultation took place on the same day they were screened for congenital portosystemic shunts at the authors' institution. Measurement of blood ammonia concentration from a venous blood sample was performed after a jugular venipuncture. On the day of the venipuncture, the Cairn terrier puppies were at least 7 weeks of age and fasted for at least 12 h. No further auscultations at the breeders' homes were performed on the Cairn terrier puppies once they had undergone echocardiography.

Dachshunds underwent echocardiographic evaluation and auscultation at various ages (median: 43 days, range: 27–49 days) by the veterinary cardiology specialist at the authors' institution. Weekly auscultations continued at the breeder's home until the puppies reached a median age of 46 days (27–49 days).

## Statistical methods

A commercially available statistical software program (RStudio version 1.1.419 PBC 2009–2018) was used for data analyses. The age of the puppies was reported in days, as a median and as a range. The interobserver agreement was evaluated by Cohen's kappa ( $\kappa$ ). Agreement was regarded as:  $\kappa \leq 0$ , poor; 0–0.20, slight; 0.21–0.4, fair; 0.41–0.60, moderate; 0.61–0.8, substantial; and  $\geq 0.81$ , almost perfect.<sup>8</sup> The uncorrected chi-square test was used to assess whether breed and gender had an influence on the presence of murmur. McNemar's test was used to evaluate whether changes in the puppies' environment had influenced the detection of the murmur. The unpaired *t*-test was used to determine whether there was a difference between the Cairn terriers and Dachshunds with respect to differences between the peak blood flow velocity of the left and right ventricular outflow tracts measured with Doppler echocardiography. Linear mixed-effects models were used to assess the association between age and murmur intensity, taking into account the repeated measurements per dog. The intercept, as well as age, were considered as both fixed and random effects. Also, a linear mixed-effects model was used to investigate whether there was a change over time in the murmur intensity according to breed (Cairn terriers versus Dachshunds), by adding the binary breed variable as well as the age-breed interaction term as fixed

effects. A *p*-value of  $<0.05$  was considered statistically significant.

## RESULTS

### Animals

The study included 12 litters, consisting of 60 puppies between 25 and 71 days of age at the time of the study period. There were six Dachshund litters from a single breeder, consisting of 28 puppies, of which 14 were males and 14 were females; and there were six Cairn terrier litters from four different breeders, consisting of 32 puppies, of which 15 were males and 17 were females. The median age of the enrolled puppies at the first auscultation was 28 days (range: 25–40 days). Auscultation was attempted on the first litter of Cairn terriers at 2 and 3 weeks of age, but their constant vocalisation at this age did not allow for the realisation of meaningful cardiac auscultation. Any examinations on puppies younger than 25 days were excluded from the study. No puppies were excluded from the study, the initial and final number of enrolled puppies was 60. All puppies were clinically healthy at the time of each evaluation. One Dachshund puppy died spontaneously during the study period after a day of acute illness of unknown origin.

### Longitudinal individual variation in murmur presence and intensity at the breeder's home

A total of 281 auscultations on 60 puppies were conducted by the veterinary cardiology specialist at the breeders' homes. The median number of auscultations per puppy at their breeder's home was 5 (range: 3–7). Of the 281 auscultations, 139 recordings were from Cairn terriers and 142 recordings were from Dachshunds. Every auscultation was compared to the previous auscultation findings for the same puppy and any changes were noted. During the observation period, a murmur was heard in 19 puppies (32%) at least once, whereas in the remaining 41 puppies, no murmur was ever detected. Of the 19 puppies with a murmur, five were Dachshunds and 14 were Cairn terriers. While murmurs were detected in 44% of the Cairn terriers, a murmur was only detected in 18% of the Dachshunds. In every Cairn terrier litter, there was at least one puppy with a murmur, whereas only half of the Dachshund litters included at least one puppy with a murmur.

Of the 19 puppies with a murmur, only two had an audible murmur on every auscultation, (both were 53 days old on final auscultation), five had murmurs that became undetectable over the observation period (at a median age of 39 days; range: 32–53 days) and 12 had an intermittent murmur. Of the two puppies with an audible murmur on each auscultation, the intensity of the murmur remained stable in one, while it fluctuated in the other.

The first round of auscultations revealed cardiac murmurs in eight of the total test population of 60 puppies (13%). The median age of those eight puppies was 26 days (range: 25–40 days), while the median age of the remaining 52 puppies was 27 days (range: 25–40 days). The median age at the time of the first auscultation of the 11 puppies who developed a detectable murmur after the first auscultation was 27 days (range: 25–31 days). For these puppies, the murmur was detected at a median age of 39 days (range: 32–53 days). In eight of these 11 puppies (73%), the murmur remained audible until the end of the observation period. In two puppies, the murmur became undetectable, and in one puppy, the murmur was intermittently audible on the subsequent auscultations.

Of the 19 puppies with heart murmurs noted at least once, all puppies had a soft (1–2/6) systolic murmur. Of the 281 auscultations performed, a murmur was present in 46 instances. The murmur intensity in six instances (from two puppies) was 2 out of 6. The intensity was graded as a 1 out of 6 in 17 instances (from 10 puppies) and the murmur was intermittently audible with a grade of 1 out of 6 on 19 auscultations (from 13 puppies).

In total, 281 auscultations were compared to previous findings from the same puppies collected at their breeders' homes a week earlier, resulting in 221 comparisons, 114 in Dachshunds and 107 in Cairn terriers. From the 221 comparisons, in 174 (79%) comparisons, no murmur was detected, whereas in 15 (7%) comparisons, a murmur was newly detectable. In nine (4%) comparisons, a murmur became undetectable and in 23 (10%) comparisons, the originally detected murmurs remained audible.

Regarding breed differences, in the Dachshunds, 106 (93%) comparisons revealed no murmur, whereas in Cairn terriers, only 68 (64%) comparisons revealed no murmur. An uncorrected two-by-two chi-square test showed that breed had an influence on the presence of an innocent murmur ( $\chi^2 = 4.6$ ,  $p = 0.031$ ), with a higher incidence in Cairn terriers. In three instances in the Dachshunds (3%) and 12 instances in the Cairn terriers (11%) with no murmur detected at the first evaluation, on a subsequent evaluation, a new murmur was detected. A previously detected murmur became undetectable in three instances in the Dachshunds (3%) and six instances in the Cairn terriers (6%). Finally, murmurs detected on the first evaluation remained audible in two instances in the Dachshunds (2%) and 21 instances in the Cairn terriers (20%).

Analysis of the total population of test subjects revealed that murmur intensity increased in 22 (10%) of the comparisons of results for multiple evaluations of a single puppy. In 15 of these comparisons, a murmur was newly detected in puppies with no murmur on initial evaluation and in the remaining seven comparisons, the intensity of an already existing murmur increased. Murmur intensity decreased in 10 (5%) comparisons. The murmur became undetectable in nine out of 10 comparisons and in one comparison the murmur persisted, but with a lower intensity. Murmur intensity stayed the same in 15 (7%) compar-

isons. No significant association was found between age and murmur intensity ( $p = 0.21$ ). The age-breed interaction term was not significant ( $p = 0.24$ ) either, indicating that Cairn terriers and Dachshunds did not significantly differ in any change in murmur intensity over time.

Of the five Dachshunds with a detectable murmur on initial auscultation, 11 of the 19 (58%) comparisons revealed no murmur on subsequent evaluation. Four (21%) comparisons showed an increase in murmur intensity (with a new murmur being detectable in three of the comparisons and increasing in intensity for the rest of the comparisons), and four (21%) comparisons showed a decrease in murmur intensity (the murmur becoming undetectable in three comparisons and decreasing in intensity in the rest of the comparisons). None of the Dachshunds had a murmur that remained unchanged in its initial intensity on subsequent auscultations.

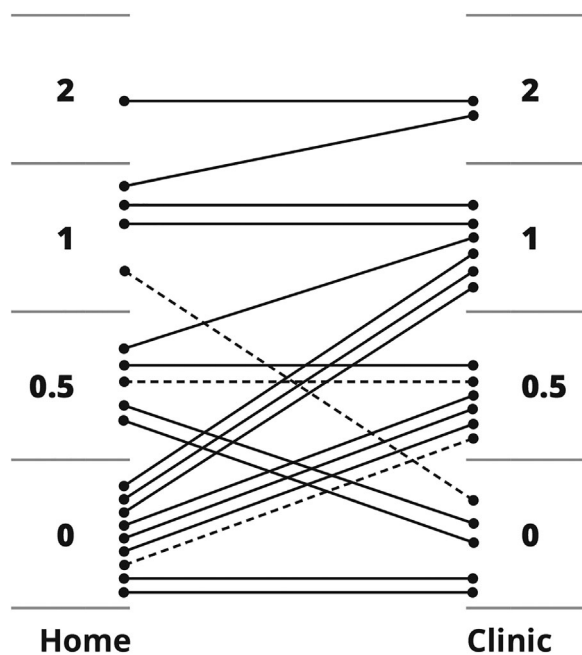
Of the 14 Cairn terriers with a detectable murmur on first auscultation, nine out of 48 (19%) comparisons revealed no murmur on subsequent auscultations. Eighteen (38%) comparisons revealed an increased murmur intensity (with a newly detectable murmur appearing in 12 comparisons and increasing in intensity in six comparisons). Six (13%) comparisons revealed a decrease in murmur intensity (with the murmur becoming undetectable in all six comparisons). In 15 (31%) comparisons, the murmur intensity remained unchanged.

## Role of gender on the presence of a murmur

Of the 19 puppies with a detectable murmur, two were female Dachshunds (11%), three were male Dachshunds (16%), four were female Cairn terriers (21%) and ten were male Cairn terriers (53%). Six of the 31 female puppies (19%) had a murmur detected during the study period, of which two were Dachshunds (14% of the 14 female Dachshunds) and four were Cairn terriers (24% of the 17 female Cairn terriers). Thirteen of the 29 male puppies (45%) had detectable murmurs during the study period, of which three were Dachshunds (36% of the 14 male Dachshunds) and 10 were Cairn terriers (67% of the 15 male Cairn terriers). An uncorrected chi-square test showed that gender had an influence on the presence of a murmur ( $\chi^2 = 4.49$ ,  $p = 0.034$ ), with a higher frequency in males.

## Role of environment on the presence and intensity of a murmur

The median age of the puppies when they underwent the echocardiographic examination and auscultation at the authors' institution was 49 days (range: 27–54 days). In the case of Cairn terriers, the median age was 55 days (range: 47–55 days) and in the case of Dachshunds, the median age was 43 days (range: 27–49 days).



**FIGURE 1** Intensity of innocent cardiac murmurs of 19 clinically healthy puppies with detectable murmurs auscultated by a veterinary cardiology specialist at the breeder's home and at the authors' institution with a median time-lapse of 2 days (range: 1–7 days) between the two evaluations. Each line represents an individual puppy. Continuous lines represent Cairn terriers and dotted lines represent Dachshunds. 0 = no murmur, 0.5 = intermittent murmur, 1 = murmur with an intensity of 1 out of 6 and 2 = murmur with an intensity of 2 out of 6

The median time elapsed between the examination that took place at the puppies' breeders' homes and at the authors' institution was 2 days (range: 0–7 days). In 43 of the 60 puppies (72%), no murmur was found in either location. In nine puppies (15%), the murmur intensity was louder at the authors' institution, whereas in three dogs (5%), the murmur intensity was louder at the breeders' home. In five puppies (8%), the murmur intensity was the same at both locations (Figure 1). McNemar's test showed that the location at which auscultation was performed (breeders' home vs. at the authors' institution) had no effect on murmur presence and intensity ( $\chi^2 = 1.6$ ,  $p = 0.206$ ).

### Auscultation findings of different observers

The auscultation findings of the veterinary cardiology specialist and the recorded auscultation findings of the first opinion veterinary practitioners were compared. For this comparison, the following two time-points were chosen: 1) when the puppies were auscultated by a first opinion veterinary practitioner at their own practices and 2) the closest date to this visit when the puppies were auscultated at their breeders' homes by the veterinary cardiology specialist. In addition, auscultation findings of the first opinion veterinary practitioners were compared to the auscultation findings of the veterinary cardiology specialist when the puppies were auscultated at the authors' institution.

As one Dachshund died in the study period before it was auscultated by a first opinion veterinary practi-

**TABLE 1** Comparison of the auscultation findings of first opinion veterinary practitioners (Veterinarians) and a veterinary cardiology specialist (Cardiologist) on 59 clinically healthy puppies. The veterinary cardiology specialist performed the auscultation at the authors' institution and the breeders' homes. The results of assessments at the breeders' homes are displayed in brackets. The median number of days between auscultation visits for individual puppies at the authors' institution was 6 days (range: 1–18 days); and, between auscultation visits at the breeders' homes versus those at the authors' institution, was 2 days (range: 0–4 days)

	Veterinarians			
	No murmur	Murmur	Total	
Cardiologist	No murmur	48 (46)	1 (0)	49 (46)
	Murmur	8 (10)	2 (3)	10 (13)
	Total	56	3	59

tioner, the findings of only 59 of the 60 enrolled puppies were compared. The median age at which the puppies were examined by a first opinion veterinary practitioner was 48 days (range: 42–53 days). Six first opinion veterinary practitioners performed auscultations of the 59 puppies.

The median number of days between auscultation by a first opinion veterinary practitioner and that by the veterinary cardiology specialist at the authors' institution was 6 days (range: 1–18 days). The median number of days between the specialist's evaluation at the authors' institution and evaluation at the breeders' homes was 2 days (range: 0–4 days). The inter-observer agreement was fair in both scenarios ( $\kappa = 0.249$  in the first and  $\kappa = 0.319$  in the second scenario).

In 46 puppies, neither the first opinion veterinary practitioners nor the veterinary cardiology specialist detected a murmur. Both the first opinion veterinary practitioners and the veterinary cardiology specialist recorded the presence of a murmur in three puppies (all Cairn terriers). In two of the puppies, the murmur intensity was judged to be the same by both evaluators (intermittent and 1 out of 6); and in the remaining puppy, the veterinary cardiology specialist found a higher murmur intensity than did the first opinion veterinary practitioner (2 vs. 1 out of 6). In 10 puppies (eight Cairn terriers and two Dachshunds) where the veterinary cardiology specialist detected a murmur, the first opinion veterinary practitioner did not detect a murmur. In no puppy did the veterinary practitioner note a murmur that had not been noted by the cardiologist (Table 1).

### Phonocardiography

Due to the limited storage capacity of the electronic stethoscope, phonocardiographic recordings were not saved in the case of one Cairn terrier puppy. In the remaining 59 puppies, 276 phonocardiograms were compared with the auscultation findings performed by the veterinary cardiology specialist on the same day with a maximum interval between evaluations of 2 min. In 17 puppies, no murmur was seen on

**TABLE 2** Comparison of interpretation of 276 phonocardiograms recorded by two independent observers (both veterinary students) on 59 clinically healthy puppies. Cohen's kappa showed almost perfect agreement ( $\kappa = 0.859$ ) on the detection of the presence or absence of a murmur. 0 = no murmur, 0.5 = intermittently visible murmur and 1 = murmur visible at every heartbeat

		Observer 1			Total
		0	0.5	1	
Observer 2	0	146	5	8	159
	0.5	5	26	2	33
	1	1	2	81	84
	Total	152	33	91	276

phonocardiograms recorded throughout the observation period, whereas murmurs were detected on phonocardiograms recorded on all the remaining 42 puppies.

Comparison of phonocardiogram interpretations by two different investigators (Donny Rigterink and Mariska A. L'Herminiez) resulted in almost perfect agreement ( $\kappa = 0.859$ , Table 2). In 253 of the 276 recordings (92%), there was an agreement between the two investigators that there was no murmur in 146 recordings, that the murmur was intermittent in 26 recordings and that the murmur was visible with each heartbeat in 81 recordings. There was a disagreement between the two investigators on 23 recordings (8%). There was disagreement on whether the murmur was intermittently visible or absent in 10 recordings (4%), on whether the murmur was absent or present at each heartbeat in nine recordings (3%), and on whether the murmur was intermittently visible or present with each heartbeat in four recordings (1%).

### Comparison of auscultation and phonocardiography results

In 30% of the auscultations where an audible murmur was not detected by the cardiology specialist, the phonocardiogram documented a murmur (Table 3). If phonocardiography was considered the gold standard for detecting innocent cardiac murmurs in puppies, the accuracy of auscultation of the veterinary cardiology specialist, in correctly detecting the presence or absence of a murmur in this study, was 68%. In the Dachshunds, this accuracy was 82% (based on 116 comparisons) and in the Cairn terriers, this accuracy was 54% (based on 72 comparisons). This low accuracy is the result of the large number of false-negative results found on auscultation as compared to phonocardiographic detection. Auscultation was determined to have high specificity with only 2% of false-positive findings.

### Echocardiography

Echocardiography detected no congenital cardiac anomalies in any of the puppies. In one puppy that had

**TABLE 3** Comparison of auscultation findings of the veterinary cardiology specialist with phonocardiograms recorded on 59 clinically healthy puppies at the breeders' homes by the same specialist within 2 min of the auscultation. (a) On all dogs (276 comparisons), (b) On the Cairn terriers (134 comparisons) and (c) On the Dachshunds (142 comparisons)

All dogs	Auscultation			
	Murmur	No murmur	Total	
Phonocardiography	Murmur	42	83	125
	No murmur	5	146	151
	Total	47	229	276
Cairn terriers	Auscultation			
	Murmur	No murmur	Total	
Phonocardiography	Murmur	36	58	94
	No murmur	4	36	40
	Total	40	94	134
Dachshunds	Auscultation			
	Murmur	No murmur	Total	
Phonocardiography	Murmur	6	25	31
	No murmur	1	110	111
	Total	7	135	142

a murmur on all phonocardiograms and no murmur on auscultation, a trivial mitral valve regurgitation jet was detected by colour Doppler echocardiography as the only possible abnormal finding.

In all puppies, pulmonic and aortic stenosis, as well as intra- and extracardiac left-to-right shunts, were excluded. The median peak blood flow velocity in the right ventricular outflow tract and pulmonic artery measured with continuous wave Doppler mode from the standard right parasternal short-axis view was 0.92 m/s (range: 0.67–1.33 m/s). The median peak blood flow velocity in the left ventricular outflow tract and aorta measured with continuous wave Doppler mode from the subcostal view was 1.32 m/s (range: 0.85–1.61 m/s). In 28 Dachshunds, the median peak blood flow velocity in the pulmonic artery and the right ventricular outflow tract was 0.83 m/s (range: 0.67–1.31 m/s). In 32 Cairn terriers, it was 0.97 m/s (range: 0.76–1.33 m/s). In 28 Dachshunds, the median peak blood flow velocity in the aorta and the left ventricular outflow tract was 1.10 m/s (range: 0.85–1.39 m/s) and in 32 Cairn terriers, it was 1.44 m/s (range: 1.05–1.78 m/s). An unpaired *t*-test revealed no significant difference between the Cairn terriers and the Dachshunds when the peak blood flow velocities in the pulmonic artery ( $p = 0.29$ ) and the aorta ( $p = 0.32$ ) were compared.

### DISCUSSION

This study detected a remarkable spontaneous week-to-week variation in the presence and intensity of innocent cardiac murmurs in 19 of the 60 enrolled puppies (five Dachshunds and 14 Cairn terriers) where a murmur was auscultated during the study period. Though all external variables (including location,

investigator and handling method) were consistent for each evaluation, varying levels of hydration state, blood viscosity and excitement levels of the enrolled puppies could have played a role. The variations in murmur presence and intensity were not related to age.

Phonocardiography detected murmurs at a much higher rate than did auscultation: in 88% versus 44% of the Cairn terriers and in 50% versus 18% of the Dachshunds. This finding can have two possible explanations: (1) the veterinary cardiology specialist was unable to detect very soft murmurs or (2) the murmurs were of inaudible intensity for the human ear. As there was only one investigator who performed all auscultations, no differentiation between these two options is possible. These results show that false-positive auscultation findings by the veterinary cardiology specialist involved in this study are very unlikely. Involving a second veterinary cardiology specialist, who would perform auscultation immediately after the first veterinary cardiology specialist auscultated each puppy, could provide more information on this aspect in future studies. The findings of this study suggest that using electronic stethoscopes with a phonocardiography option as a screening method is likely to lead to the detection of murmurs in more puppies than does the use of acoustic stethoscopes alone. However, because echocardiography showed no abnormalities in any of the enrolled puppies, using phonocardiography in practice is unlikely to result in any clinically useful conclusions. As such, the authors do not recommend phonocardiography for cardiac screening in puppies as clinically irrelevant murmur detection could result in unnecessary concerns for the owners.

Innocent murmurs were more prevalent in Cairn terriers than in Dachshunds, and in males compared to females. Potential reasons for this finding remain unclear as peak blood flow velocities in the left and right ventricular outflow tracts showed no breed- or sex-related differences. Results of published studies evaluating the prevalence of innocent murmurs in Cairn terriers yielded similar outcomes when compared to those of this study.<sup>1,3,5</sup>

In the present study, the stress of transportation to and evaluation in a location outside the breeders' home environment did not seem to influence the presence or intensity of innocent murmurs in a predictable way. A previous study evaluating Boxer dogs without a murmur or with a low-intensity systolic murmur found an increase in murmur duration on phonocardiography and an increase in aortic flow velocity as measured by Doppler echocardiography when stress was induced by a squeaky toy and a barking sound.<sup>9</sup> The change of location in the present study seemed to have less impact on the puppies' stress levels than did the auditive stimulants used in the published Boxer study.

The auscultation findings of the first opinion veterinary practitioners and the veterinary cardiology specialist showed fair agreement regardless of whether the auscultation took place at the breeders' homes or the authors' institution. Given that the interval between

auscultations by the first opinion veterinarian and the cardiology specialist was variable (several days of difference were possible between one test subject and another), it is difficult to hypothesize as to the reason for the variability in their clinical findings. Potential explanations include the spontaneous week-to-week variation of the murmurs or the auscultation skills (i.e., experience) of the individual veterinarians.<sup>5,9</sup> However, the fact that the cardiology specialist detected murmurs in more puppies than did the veterinary practitioners (Table 1) suggests that practice and training in cardiac auscultation could be a contributing factor. This question could be better assessed in a future study by evaluating puppies with congenital cardiac anomalies in which no spontaneous short-term variation in murmur intensity is expected.

Our study showed almost perfect agreement ( $\kappa = 0.859$ ) between the two observers when phonocardiogram interpretation was used. This finding suggests that phonocardiography could be a useful additional test in the case of equivocal auscultation findings, provided that the recorded phonocardiograms are of good quality.<sup>10</sup>

The present study has some limitations, the most important being the relatively small number of dogs (19 of a total of 60) evaluated as having a detectable murmur. Auscultation findings of a second veterinary cardiology specialist could have provided a more objective comparative evaluation of the presence and intensity of murmurs in the test subjects.

We conclude that there was remarkable, spontaneous, week-to-week variation in the presence and intensity of innocent cardiac murmurs within the population of test subjects resulting in detected murmurs that became undetectable and then seemingly reappeared, on a weekly basis, in an unpredictable way. This change did not appear to be affected by stress caused by a changing testing environment. Discrepancies in the auscultation findings of different veterinarians in puppies with innocent cardiac murmurs might also be explained by spontaneous individual variations in the presence and intensity of cardiac murmurs in the puppies evaluated.

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## AUTHOR CONTRIBUTIONS

Viktor Szatmári was responsible for the conception and design of the study, acquisition of data and revising the manuscript. Donny Rigterink and Mariska A.

L'Herminez performed analysis and interpretation of data, and they drafted the manuscript.

### ETHICS STATEMENT

This study was conducted under ethical approval of the Animal Welfare Body of the Utrecht University. The animals were handled according to high ethical standards and national legislation.

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No funding was received for this study.


### CONFLICT OF INTEREST

The authors declare to have no conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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