

STANDARD ARTICLE

Left heart dimensions in anemic cats and dogs before and after blood transfusion

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Abstract

Background: Whether anemic cats and dogs with increased left heart dimensions are at higher risk of transfusion-associated circulatory overload, and the effect of blood transfusion on left heart dimensions in naturally occurring anemia is unknown.

Hypothesis/objectives: To evaluate the effect of blood transfusion on left heart dimensions in clinically relevant anemia.

Animals: Twenty dogs and 20 cats presenting to a university veterinary teaching hospital.

Methods: In this prospective observational study, anemic dogs and cats requiring blood transfusion were included. Packed cell volume (PCV), total solids, and echocardiography were performed before and within 24 hours of blood transfusion. Signalment, bodyweight, disease process, transfusion duration and volume, and prior treatments were recorded. Nonparametric statistics were reported as median [range]. Post hoc Bonferroni correction set significance at $P < .006$.

Results: After transfusion, PCV increased in cats (12% [6–16] to 18% [10–33], $P = .001$) and dogs (14% [7–24] to 25% [9–37], $P = .001$), heart rate decreased in dogs (104 bpm [86–166] to 87 bpm [56–138], $P < .001$), and fractional shortening decreased in cats (57.1% [36.0–84.7] to 41.0% [28.1–69.6], $P = .002$) and dogs (33.79% [19.33–62.79] to 31.89% [19.06–51.47], $P = .006$). Left ventricular internal diameter in systole increased in cats (6.5 mm [2.7–9.8] to 7.9 mm [5.3–11.1], $P = .001$). Normalized left ventricular internal diameter in diastole (1.48 [1.25–1.79] to 1.57 [1.33–2.00], $P = .001$) and systole (0.87 [0.58–1.19] to 1.00 [0.74–1.36], $P = .001$) increased in dogs. Incidence of volume overload did not differ before (14/20 cats, 70%; 9/20 dogs, 45%) or after (12/20 cats, 60%; 11/20 dogs, 55%) transfusion ($P = .64$).

Abbreviations: FS%, fractional shortening; HR, heart rate; IMHA, immune mediated hemolytic anemia; IVSd, interventricular septum thickness at end-diastole; LA : Ao, left atrial diameter : aortic diameter ratio; LA : AV, longitudinal left atrial diameter indexed to aortic valve; LAD Max, maximal left atrial diameter; LVFWd, left ventricular free wall thickness in end-diastole; LVIDD, left ventricular internal diameter in diastole; LVIDDN, bodyweight-normalized left ventricular internal diameter in diastole; LVIDs, left ventricular internal diameter in end-systole; LVIDSN, bodyweight-normalized left ventricular internal diameter in systole; LVWT Max, maximal left ventricular wall thickness; PCV, packed cell volume; TACO, transfusion-associated circulatory overload; TS, total solids.

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Conclusions and clinical importance: Blood transfusion is well tolerated when signs of volume overload are present before transfusion.

KEYWORDS

euvolemia, hemolysis, hemorrhage, hypovolemia, isovolemia, normovolemia, transfusion-associated circulatory overload

1 | INTRODUCTION

Blood transfusions are performed frequently on an emergency basis in dogs and cats with clinically relevant anemia. Transfusion reactions are recognized complications of blood product administration and include nonimmunologic reactions such as transfusion-associated circulatory overload (TACO), which leads to congestive heart failure. No veterinary consensus exists on the definition of TACO, but the human literature defines it as a combination of acute respiratory distress, tachycardia, acute or worsening pulmonary edema, and positive fluid balance (including cavitory effusions) occurring during or within 6 hours of blood transfusion.^{1,2}

Anemia induces numerous compensatory mechanisms in order to maintain adequate tissue oxygen delivery. After initial alterations in oxygen offloading to tissues and erythropoiesis, activation of the renin-angiotensin-aldosterone system and arginine vasopressin release act to retain water and maintain intravascular volume.³ Cardiac afterload is reduced by decreased blood viscosity, and hypoxia and nitric oxide mediated vasodilation.⁴ In acute or severe chronic anemia catecholamine and non-catecholamine factors increase cardiac output by changes in heart rate (HR) and stroke volume.³⁻⁶ Eventually increased intravascular volume leads to increased cardiac preload, and atrial natriuretic peptide release paradoxically mediates further vasodilation.³ Left ventricular hypertrophy, diastolic dysfunction, and left-sided congestive heart failure can occur as a result of these neurohormonal responses to anemia in humans.^{4,7,8}

There are similar neurohormonal responses to anemia in dogs and cats as is reported in humans. Left ventricular and left atrial dimensions increase in severely anemic cats.^{9,10} Experimental models of euvoletic anemia in dogs identify statistically significant decreases in total peripheral resistance and systolic, mean and diastolic blood pressures, suggesting that there is vasodilatation associated with anemia.¹¹ Significant increases in ejection fraction also suggest increased left ventricular performance in compensation for acute experimentally induced anemia.¹² Experimental models of euvoletic anemia identify increased blood flow velocity by Doppler ultrasound in the abdominal aorta and splanchnic vessels.¹³ It is unknown if these hemodynamic responses place cats and dogs at higher risk of TACO. There are currently no prospective veterinary studies evaluating the frequency of volume overload in dogs or cats with naturally occurring anemia.

The objectives of this study were to evaluate the effect of blood transfusion on left heart dimensions in both dogs and cats with clinically relevant anemia, to compare left heart dimensions in the same individuals following resolution of their anemia and to evaluate the frequency of volume overload in dogs and cats before and after blood transfusion. It was hypothesized that anemic cats would demonstrate increased left ventricular and left atrial dimensions as previously

reported but that there would be no significant change between echocardiographic variables before and after transfusion. Existing experimental models and anecdotal experience suggest that changes in left heart dimensions may be less pronounced in dogs, and therefore for dogs null hypothesis was assumed (that there would be no significant change in echocardiographic variables at any time point).

2 | MATERIALS AND METHODS

Cats and dogs presenting to the Queen Mother Hospital for Animals' emergency room were eligible for inclusion if they received a blood transfusion for clinically relevant anemia (packed cell volume [PCV] <24% in cats, PCV <30% in dogs) and client consent for study participation was obtained. Exclusion criteria were lack of owner consent, patient fragility (patient instability such that echocardiographic examination would be detrimental as deemed by the attending clinician) or previous history of any cardiac disease.

Cats and dogs were included if they received a blood transfusion (canine packed red blood cells, feline packed red blood cells, feline whole blood, or xenotransfusion). The type, volume, and rate of blood transfusion administration were determined by the attending clinician. The attending clinician had access to the echocardiographic findings and had full autonomy to determine the patient's treatment. Cats and dogs were AB and DEA 1 blood typed, respectively, and with the exception of xenotransfusions were administered type-matched blood transfusions.

Two-dimensional (2D) and M-mode transthoracic echocardiography was performed by a trained observer before and within 24 hours after blood transfusion. Posttransfusion echocardiography was scheduled for 12 hours after completion of blood transfusion; however, variability was permitted to account for time of day and availability of the service. In cats, 2D imaging of the right parasternal long axis 4- and 5-chamber views, and right parasternal short axis views were acquired.¹⁴ For dogs, the same views were taken with additional M-mode imaging of the left ventricle using the right parasternal short axis view.¹⁴ The echocardiogram was subsequently reviewed and measurements were taken by a single observer, who was blinded from the clinical data including the PCV/total solids (TS). Each echocardiographic variable was measured over 3 different cardiac cycles and averaged. For left ventricular dimensions, interventricular septal thickness at end-diastole (IVSd), left ventricular free wall thickness in end-diastole (LVFWd), left ventricular internal diameter in end-diastole (LVIDd), left ventricular internal diameter in end-systole (LVIDs), and left ventricular fractional shortening (FS%) were measured using 2D imaging for cats and M-mode for dogs.^{14,15} To

account for body size in dogs, allometric scaling was used for left ventricular dimensions.¹⁶ In cats, maximal left ventricular wall thickness (LVWT Max) was recorded as the greater of the averaged measures of septal or free wall thickness.¹⁷ For left atrial dimensions, left atrial diameter : aortic diameter ratio (LA : Ao) and maximal left atrial diameter (LAD Max) were taken in both species as previously described.^{17,18} In dogs, LAD Max was indexed to aortic valve in right parasternal long axis 5-chamber view to account for the variation in body size.¹⁹

Left heart volume overload was defined as the presence of any of the following criteria: LAD Max >1.6 cm, LA : Ao >1.5, or LVIDd >2.0 cm for cats; longitudinal LA indexed to aortic valve (LA : AV) >2.6, LA : Ao >1.5, or bodyweight-normalized left ventricular internal diameter in diastole (LVIDDN) >1.7 in dogs.^{9,19} Left ventricular hypertrophy in cats was defined as LVWT Max of 6 mm or greater.

All measurements were recorded before and after transfusion, in addition to measurements of PCV, TS, and HR before and after transfusion. After transfusion measurements were collected 12 hours after completion of the blood transfusion. Signalment, bodyweight, transfusion volume (total and ml/kg), duration of transfusion, pretransfusion treatment with steroids or IV fluids before or since hospital admission, and primary disease process were also recorded. Transfusion records were reviewed for new onset tachypnoea or documentation of acute respiratory distress. Cats and dogs were considered to have TACO if after transfusion they had volume overload status on echocardiography with evidence of tachypnoea, pleural or pericardial effusion, or increased respiratory effort documented.

2.1 | Statistical analysis

A sample size calculation was performed to determine the number of cases needed to demonstrate significant difference between normal and

overloaded volume status with 80% power and 95% confidence intervals. Eighteen enrolments were required based on the statistical data available from existing study samples.⁹ Statistical analysis was performed separately on dogs and cats as existing literature suggests that they may have different hemodynamic responses to anemia and blood transfusion. The aim therefore was to recruit 20 cats and 20 dogs. Commercially available statistical software (IBM SPSS Statistics, Version 24, IBM United Kingdom Limited, Hampshire, United Kingdom) was used to assess for data normality. Wilcoxon-signed rank test was performed to compare variables and a post hoc Bonferroni correction among echocardiographic variables set significance at $P < .006$. Effect of treatment on pretransfusion variables was assessed with a Kruskal-Wallis independent samples test. A related samples McNemar test compared left heart overload pretransfusion and post-transfusion. Values were reported as median [range].

3 | RESULTS

3.1 | Patient population

Twenty-one cats and 24 dogs were enrolled in the study between July 2017 and July 2018. One cat was excluded because of poor compliance, and 4 dogs were excluded as an echocardiogram after transfusion was not performed.

The feline population had a median age of 4.07 years [1.18-14.7] and a median bodyweight of 3.37 kg [2-7]. Domestic short hair was the predominant breed (60%, $n = 12$) with other breeds represented including Siamese ($n = 2$), and 1 each of domestic long hair, domestic medium hair, British shorthair, Maine coon, Persian, and British blue. Three cats were anemic because of hemorrhage (2 with hemoperitoneum, 1 with gastrointestinal hemorrhage), 3 cats were

TABLE 1 Echocardiographic variables, packed cell volume, and heart rate before and after blood transfusion in cats ($n = 20$ unless otherwise stated).

Variable	Before transfusion median (range)	After transfusion median (range)	P value
PCV (%)	12 (6-16)	18 (10-33) (n = 18)	.001*
TS (g/l)	76 (50-92) ($n = 19$)	78 (50-89) ($n = 11$)	.86
HR (bpm)	204 (184-271)	196 (120-225)	.12
IVSd (mm)	4.7 (3.7-6.3)	4.6 (3.8-6.8)	.23
LVIDd (mm)	15.7 (11.1-17.9)	15.4 (11.0-19.4)	.58
LVFWd (mm)	4.3 (3.6-6.8)	4.6 (3.1-8.4)	.82
LVIDs (mm)	6.5 (2.7-9.8)	7.9 (5.3-11.1)	.001*
FS%	57.1 (36.0-84.7)	41.0 (28.1-69.6)	.002*
LAD Max (mm)	16.6 (13.8-21.9)	17.7 (11.6-22.4)	.59
LA:Ao	1.56 (1.23-1.77)	1.49 (0.95-2.0)	.27
LVWT Max (mm)	5.05 (4.10-7.20)	5.20 (3.70-7.20)	.12
Volume overload	14/20 (70%)	12/20 (60%)	.63

Abbreviations: FS%, fractional shortening; HR, heart rate; IVSd, interventricular septal thickness at end-diastole; LA : Ao, left atrial diameter : aortic diameter ratio; LAD Max, maximal left atrial diameter; LVFWd, left ventricular free wall thickness in end-diastole; LVIDd, left ventricular internal diameter at end-diastole; LVIDs, left ventricular internal diameter at end-systole; LVWT Max, maximal left ventricular wall thickness; PCV, packed cell volume; TS, total solids.

*Statistical significance ($P < .006$).

Statistically significant values are represented in bold.

Variable	Before transfusion median (range)	After transfusion median (range)	P value
PCV (%)	14 (7-24)	25 (9-37) (n = 11)	.001*
TS (g/L)	61 (42-86) (n = 18)	60.5 (54.0-72.0) (n = 7)	.91
HR (bpm)	104 (86-166)	87 (56-138)	<.001*
LVIDDN	1.48 (1.25-1.79)	1.57 (1.33-2.00)	.001*
LVIDSN	0.872 (0.58-1.19)	1.00 (0.74-1.36)	.001*
FS%	33.79 (19.33-62.97)	31.89 (19.06-51.47)	.006*
LAD Max (mm)	36.3 (24.1-51.4)	38.1 (26.3-51.7)	.14
LA:Ao	1.38 (1.14-1.72)	1.37 (1.17-1.70)	.75
LA:AV	2.35 (1.90-2.70)	2.40 (2.00-2.80)	.011
Volume overload	9/20 (45%)	11/20 (55%)	.63

Abbreviations: FS%, fractional shortening; HR, heart rate; LA : Ao, left atrial diameter : aortic diameter ratio; LA : AV, longitudinal left atrial diameter indexed to aortic valve; LAD Max, maximal left atrial diameter; LVIDDN, normalized left ventricular internal diameter at end-diastole; LVIDSN, normalized left ventricular diameter at end-systole; PCV, packed cell volume; TS, total solids.

*Statistical significance ($P < .006$).

Statistically significant values are represented in bold.

	Steroid treatment		IV fluid treatment	
	Dogs (n = 18)	Cats (n = 18)	Dogs (n = 16)	Cats (n = 18)
Number receiving treatment before transfusion	8/18	2/18	7/16	2/18
	<i>P</i> values			
PCV	.98	.60	.50	.45
TS	.39	.85	.48	.10
HR	.40	.98	.65	.42
LVIDd	.51	.15	.67	.26
LVIDs	.19	.92	.84	.45
FS%	.17	.48	.93	.15
LAD Max	.60	.68	.60	.36
LA:Ao	.75	.60	.38	.51
LVIDDN	.63	-	.33	-
LVIDSN	.27	-	.94	-
IVSd	-	.83	-	.84
LVWT Max	-	.66	-	.34

Note: *P* values represent comparison between dogs and cats that did and did not receive treatment with corticosteroids and IV crystalloid fluids pretransfusion.

Abbreviations: FS%, fractional shortening; HR, heart rate; IVSd, interventricular septal thickness at end-diastole; LA : Ao, left atrial diameter : aortic diameter ratio; LA : AV, longitudinal left atrial diameter indexed to aortic valve; LAD Max, maximal left atrial diameter; LVIDd, left ventricular internal diameter at end-diastole; LVIDs, left ventricular internal diameter at end-systole; LVIDDN, normalized left ventricular internal diameter at end-diastole; LVIDSN, normalized left ventricular diameter at end-systole; LVWT Max, maximal left ventricular wall thickness; PCV, packed cell volume; TS, total solids. *Statistical significance ($P < .006$).

diagnosed with a form of leukemia and the remaining 14 cats had immune-mediated hemolytic anemia (IMHA), which was primary in 13 patients. Primary IMHA was diagnosed in these patients after demonstrating compatible erythrocyte morphological abnormalities and

TABLE 2 Echocardiographic variables, packed cell volume and heart rate before and after blood transfusion in dogs (n = 20 unless otherwise stated).

TABLE 3 Effect of pretransfusion therapies on pre transfusion clinical and laboratory parameters, and echocardiographic variables in dogs and cats

failing to identify an underlying disease process by hematology, biochemistry, urine analysis, abdominal and thoracic imaging, and infectious disease testing. One cat with primary IMHA initially presented with concurrent *Mycoplasma haemominutum* but demonstrated

relapse of IMHA after treatment of the *M. haemominutum*. The cat with secondary IMHA patient was diagnosed with hepatic and splenic neoplasia.

The canine population had a median age of 8.15 years [5.21-12.25] and a median bodyweight of 12.45 kg [6.1-33.6]. Breeds represented were crossbreeds (n = 4), English cocker spaniel (n = 3), springer spaniel (n = 2), Jack Russell terrier (n = 2), Labrador retriever (n = 2), and 1 each of lurcher, Staffordshire bull terrier, greyhound, boxer, miniature dachshund, shih tzu, and Airedale terrier. Nine dogs were diagnosed with IMHA, which was primary in 6 cases, and secondary to hepatic neoplasia (n = 1) and gastric neoplasia (n = 1). One dog with IMHA had concurrent Fanconi syndrome. Five dogs were transfused because of hemorrhage; 2 had gastrointestinal hemorrhage because of intestinal lymphoma (n = 1) and immune-mediated thrombocytopenia (n = 1), 2 had hemoperitoneum secondary to a bleeding splenic neoplasm, and 1 had intercapsular bleeding into both a cardiac and splenic mass. Four dogs had anemia because of decreased erythrocyte production from precursor targeted immune-mediated anemia (n = 1), acute lymphoblastic leukemia (n = 1), lymphoma (n = 1), and neoplasia that was not further characterized as the patient was euthanized (n = 1). In 2 dogs, a definitive diagnosis was not reached.

3.2 | Treatments

Cats received blood transfusions for a median duration of 7 hours 5 minutes [20 minutes to 16 hours 45 minutes] with a median volume delivered of 13.8 mL/kg [7.2-18.7]. Nine patients received feline packed red blood cells, 7 had feline fresh whole blood, and 5 cats received a xenotransfusion of canine packed red blood cells. Eleven percent (2/18) of cats received treatment with

corticosteroids before transfusion and 11% (2/18) received isotonic crystalloids. Neither treatment significantly affected left heart dimensions before transfusion (Table 3).

The median duration of blood transfusion in dogs was 5 hours 22 minutes [2 hours 20 minutes to 7 hours] and the median volume delivered was 11.95 mL/kg [6.3-22.9]. All dogs received canine packed red blood cells. A value of 44.4% (8/18) of dogs received treatment with corticosteroids before transfusion and 43.8% (7/16) received isotonic crystalloids. Neither treatment significantly affected left heart dimensions before transfusion (Table 3).

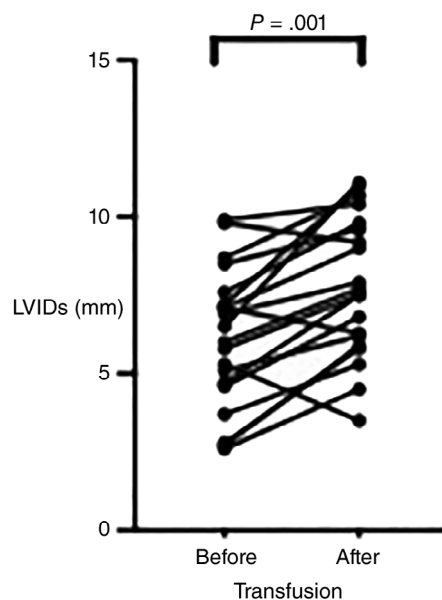


FIGURE 2 Left ventricular internal diameter in systole (LVIDs) in anemic cats before and after blood transfusion

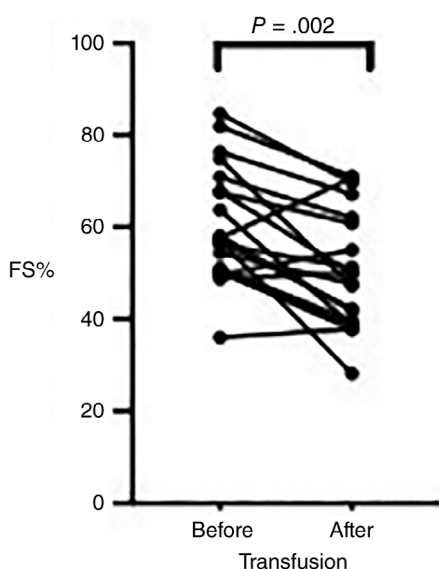


FIGURE 1 Fractional shortening (FS%) in anemic cats before and after blood transfusion

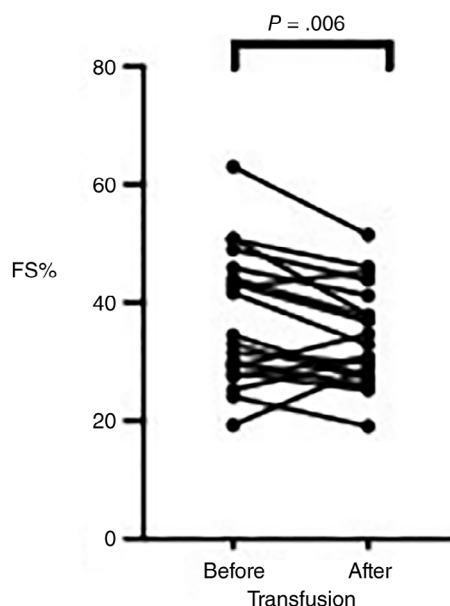


FIGURE 3 Fractional shortening (FS%) in anemic dogs before and after blood transfusion

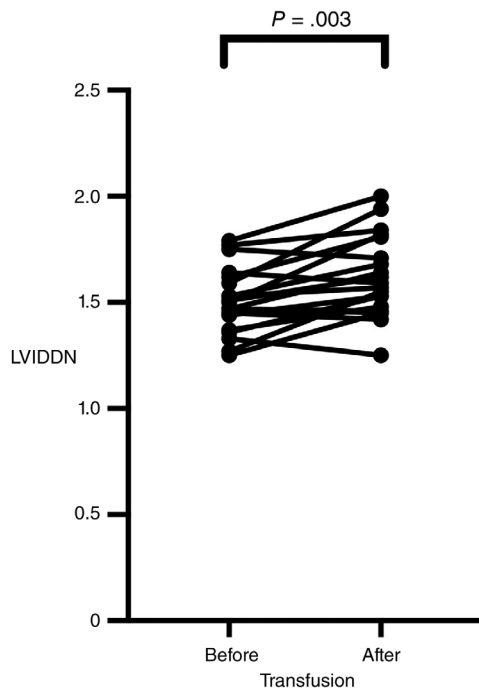


FIGURE 4 Normalized left ventricular internal diameter in diastole (LVIDDN) in anemic dogs before and after blood transfusion

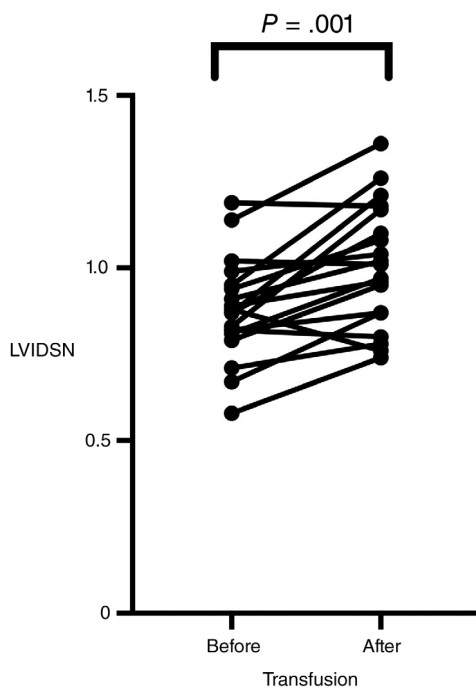


FIGURE 5 Bodyweight-normalized left ventricular internal diameter in systole (LVIDSN) in anemic dogs before and after blood transfusion

3.3 | Clinical and laboratory variables

Packed cell volume significantly increased after transfusion in both dogs and cats ($P = .001$). Total solids were not significantly affected

by transfusion (Tables 1 and 2). Heart rate decreased significantly after transfusion in dogs ($P < .001$) but not cats ($P = .117$).

Three dogs had an increase in respiratory rate from baseline; they were either panting or had respiratory rates below 40 breaths per minute. No dogs had an increase in respiratory effort. No cats had an increase in respiratory rate or effort documented.

3.4 | Echocardiographic variables

A total of 14 cats (70%) and 9 dogs (45%) were classified as volume overloaded before transfusion, compared to 12 cats (60%) and 11 dogs (55%) that fulfilled criteria for volume overload after transfusion. One cat (5%) and 3 dogs (15%) without volume overload before transfusion were classified as volume overloaded after transfusion. Volume overload status resolved after transfusion in 3/14 cats (21.4%) and 1/9 dogs (11.1%). There was no significant difference in volume overload status after blood transfusion in either cats ($P = .63$) or dogs ($P = .63$).

After transfusion, FS% decreased significantly ($P = .002$, Figure 1) and LVIDs increased significantly in cats ($P = .001$, Figure 2). No other echocardiographic variables were significantly different after transfusion in cats (Table 1). One cat was deemed to have TACO, as it had a small volume pericardial effusion with no cardiac tamponade on echocardiogram after transfusion. This cat also fulfilled the criteria for left heart volume overload before and after transfusion, and on follow up echocardiography. This cat had left ventricular hypertrophy before and after transfusion. Left ventricular hypertrophy was also documented in 2 other cats (3/20, 15%). No other cats or dogs had documented pleural or pericardial effusion before or after transfusion.

After transfusion in dogs, FS% decreased significantly ($P = .006$, Figure 3), as did normalized left ventricular internal diameter in diastole ($P = .003$, Figure 4) and systole ($P = .001$, Figure 5) (Table 2). No other echocardiographic variables were significantly different post-transfusion in dogs.

4 | DISCUSSION

In this study, left ventricular diameters in systole and diastole increased in both dogs and cats after transfusion. These findings are similar to those of a retrospective study evaluating anemic cats.⁹ There are many possible explanations for this finding including decreased left ventricular workload after improved oxygen carrying capacity; increased blood viscosity with increased erythrocyte concentration; or increased volume after transfusion delivery. Blood transfusion (and prior treatment with isotonic crystalloids) provides an exogenous source of intravascular volume expansion. Neurohormonal mechanisms are deactivated very quickly after restoration of renal tissue oxygen delivery; however, it is unclear how quickly this translates to normalized blood volume in dogs and cats.³

Despite increasing intravascular volume through the administration of blood products, there was no significant increase in the presence of volume overload after transfusion even though the majority

of anemic cats and dogs (70% and 45%, respectively) presented with left heart dimensions suggestive of volume overload. None of these cats or dogs presented with clinical signs of congestive heart failure and only 1 developed circulatory overload despite the incidence of volume overload remaining high (60% cats and 55% dogs). The clinical incidence of volume overload has been recognized but its clinical relevance has not been directly assessed before. The failure of these findings to manifest as TACO in the majority suggests that this sample tolerated blood transfusion, and that standard rates and volumes of blood product administration are appropriate for cats and dogs with euvoletic anemia.

Three cats had increased left ventricular wall thickness. Only 1 of these cats developed a small pericardial effusion consistent with TACO after transfusion, but there was no tachypnea or respiratory distress during the transfusion period. Although the temporal association and resolution of pericardial effusion led us to believe that it was a transudate because of left-sided congestive heart failure, the effusion was not sampled because of the small volume. The cat had been diagnosed with primary IMHA, but sterile inflammatory, septic, neoplastic, and hemorrhagic effusions were not excluded. The prevalence of hypertrophic cardiomyopathy (HCM) phenotype cats is consistent with previous studies,^{9,20} so the likelihood of volume overload is translatable to the general population. As this was the only cat to develop signs of TACO, it is possible that blood transfusions might need to be administered cautiously and with additional monitoring in cats with HCM or existing cardiac disease.

The normalization in FS% supports that anemic cats and dogs are in a hyperdynamic state initially which improves after blood transfusion. There is increased fractional shortening and decreased peripheral vascular resistance in experimental and clinical studies of anemia in cats and dogs.^{11,20,21} These findings would be expected with decreased blood viscosity and vasodilatation in anemic cats and dogs; hemodynamic changes that resolve quickly after blood transfusion.

Left atrial dimensions were not significantly affected by transfusion in this study sample. It is possible that this sample did not have passive dilatation if their disease was not sufficiently chronic or severe. Neurohormonal mechanisms are activated early in anemia, but increased preload is typically a late finding in anemic humans.²²

Data on normal left heart dimensions in dogs were published after this study was completed.²³ Based on these data, definitions of left heart volume overload would be different to the current study and may affect the classification of dogs considered to have TACO. Using the updated allometric equation and reference intervals, dogs would be considered volume overloaded if they met any of the following: normalized LVIDd >1.63, normalized LAD Max >1.56, or LA : Ao >1.68. Post hoc application of this criteria to this study sample does not affect the classification of dogs considered volume overloaded.

Limitations to this study pertain largely to its observational nature. Compensatory mechanisms are complex and multifactorial, therefore assessing only echocardiographic variables does not comprehensively assess clinical response to blood transfusion. Invasive hemodynamic monitoring is neither practical nor safe in severely

anemic cats or dogs. Blood pressure was not assessed in the current sample as interpretation could be confounded by patient stress.

The study sample is heterogenous with differences in etiology and disease chronicity. This study would be underpowered to detect a difference between etiologies. The findings of this study are likely still relevant to the emergency clinician as these challenges realistically reflect the clinical setting. A large proportion of cats were diagnosed with primary IMHA, which is consistent with reported demographics.²⁴

There was also a large variability in treatment. All cats and dogs were referred from other hospitals so initial treatment could not be standardized. It was also unclear from the provided medical records exactly what volume of isotonic crystalloids patients that were treated with fluids received. Based on the lack of difference in cats and dogs that were or were not treated with IV fluids before transfusion, it is unlikely that the volume of fluids received would be sufficient to alter left heart variables. Statistical analysis also did not detect a significant difference between cats and dogs that received fluids and those that did not. Duration of blood transfusion was also highly variable. This is because treatment was at the attending clinician's discretion. At this hospital, xenotransfusions and feline blood transfusions are often aseptically divided into several syringes, with syringes administered sequentially and those not being administered stored at 4°C in a dedicated blood fridge. This permits a transfusion duration of up to 24 hours after breach of the unit.

The most severely affected dogs and cats presenting to the hospital were unstable and could not be recruited. In humans, compensatory changes correlate with anemia chronicity and severity, so this study may underestimate the severity of echocardiographic changes.^{3,4}

Echocardiography after transfusion may not detect the true extent of compensation as although PCV increased, it rarely normalized. This likely reflects an ongoing primary disease process at the time of echocardiography after transfusion, as dogs and cats are likely to receive blood transfusion to enable diagnostic testing in clinical settings. Although attempts were made to perform echocardiography at a persistent timepoint 12 hours after transfusion, this was sometimes not feasible because of the time of day or because of the additional demands for the equipment and personnel. These inconsistencies could lead to some variability in results. The timing of echocardiograms before transfusion was also not standardized, but there was less variability and therefore less likely to be clinically relevant.

The study was only single-blinded. Because the attending clinician could request the echocardiographic report, these results might have influenced treatment decisions, including transfusion duration and volume.

Unfortunately, a high number of cats and dogs in this sample died, preventing comparison of before and after transfusion variables at follow up to a "normal" baseline. This has limited the study's ability to detect the individual response to both anemia (before transfusion) and the cardiovascular response to the volume administered during blood transfusion (after transfusion). As normalized bodyweight variables were used from previously validated values for dogs, it is likely that meaningful conclusions can still be drawn from this cohort. However, the characterization of left heart overload may be arbitrary and

dogs and cats may have been misclassified. There were numerous English Springer spaniels in this study and separate left heart dimensions have been reported for this breed.²⁵ There is also the possibility of individual variation outside of these reference intervals.

ACKNOWLEDGMENTS

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

ETHICS STATEMENT

This study was approved by the Clinical Research Ethical Review Board at the Royal Veterinary College (URN M2016 0104).

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Approved by the Clinical Research Ethical Review Board at the Royal Veterinary College (URN M2016 0104).

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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