# Risk factors for transfusion-associated complications and nonsurvival in dogs receiving packed red blood cell transfusions: 211 cases (2008–2011)

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**Objective**—To determine whether the number, volume, or age of transfused packed RBC units; volume of other blood products; or pretransfusion PCV was a risk factor for transfusion-associated complications or nonsurvival in dogs.

**Design**—Retrospective case series.

**Animals**—211 client-owned dogs receiving stored packed RBC transfusions.

**Procedures**—Information collected or calculated from the medical record of each dog included the total number, volume, and dose of packed RBC units; mean age of packed RBC units; number of packed RBC units > 14 days old; age of oldest packed RBC unit; volume and dose of other blood products used; pretransfusion PCV; acute patient physiologic and laboratory evaluation score; transfusion-associated complications; and outcome.

**Results**—The dose (mL/kg) of other blood products transfused was a risk factor for transfusion-associated complications (OR, 1.03; 95% confidence interval [CI], 1.01 to 1.05). The pretransfusion PCV (OR, 1.13; 95% CI, 1.06 to 1.21) and dose of packed RBCs administered (OR, 1.04; 95% CI, 1.02 to 1.07) were risk factors for nonsurvival. Age of transfused packed RBC units was not identified as a risk factor for transfusion-associated complications or nonsurvival, but the study was statistically underpowered to detect this finding.

**Conclusions and Clinical Relevance**—Administration of larger doses of other non–packed RBC blood products was a risk factor for transfusion-associated complications, and a higher pretransfusion PCV and larger dose of packed RBCs administered were risk factors for nonsurvival. Prospective randomized studies are needed to determine whether conservative transfusion strategies will reduce transfusion-associated complications and improve outcome in dogs. (*J Am Vet Med Assoc* 2014;244:431–437)

Transfusion of packed RBC units is performed commonly in hospitalized dogs with anemia caused by hemorrhage, hemolysis, or ineffective erythropoiesis.[1,2] Some veterinary studies have associated blood administration with complications, including transfusion reactions,[1–3] postoperative pulmonary complications,[4] and increased risk of intestinal anastomosis site dehiscence.[5] Large retrospective studies[1,2] in dogs suggest that packed RBC or whole blood transfusions are associated with a 3.3% to 13% incidence of transfusion reactions; the incidence of transfusion reactions increases to 40% in dogs requiring massive transfusions.[3] One study[2] investigated the pretransfusion PCV, cause of anemia, and total dose of blood transfused as risk factors for death in dogs requiring packed RBC or whole blood transfusions, and the study found no relationship between those factors and outcome (survival to discharge from the hospital vs nonsurvival).

### ABBREVIATIONS

| | |
|---|---|
| AKI | Acute kidney injury |
| ALI | Acute lung injury |
| APPLE | Acute patient physiologic and laboratory evaluation |
| CI | Confidence interval |
| FFP | Fresh frozen plasma |

However, the dose and age of packed RBC transfusions has become a great point of controversy in human medicine, which has led to the investigation of conservative transfusion triggers and other transfusion strategies to mitigate the occurrence of transfusion-associated complications.[6–8] The effect of storage on RBC function and the incidence of transfusion-associated complications or death have been heavily investigated in human medicine during the past 10 years and have been reviewed extensively in the literature.[9,10] Results of several retrospective human studies[11–17] indicate that increasing the duration of storage of packed RBC units prior to transfusion is associated with an increased duration of hospitalization as well as an increased incidence of infection, AKI, ALI, and other complications, including death. However, other human studies[18,19] have not found an association between the age of packed RBC units administered and death.

Although the association between age of stored packed RBC units and outcome remains controversial, the number of packed RBC units transfused to human patients is consistently associated with increased rates of morbidity and death.[19–21] Some human studies[19,21] even reveal that the risk of death or other adverse outcomes increases with every unit of packed RBCs administered. Likewise, several human studies[6–8,22] support the use of a conservative or restrictive transfusion strategy, which involves use of a lower hemoglobin concentration (< 7 g/dL) to trigger a packed RBC transfusion, as opposed to a liberal or standard transfusion strategy that uses a higher hemoglobin concentration (< 9 to 10 g/dL). These studies[6–8,22] reveal that use of a conservative transfusion trigger (ie, lower pretransfusion PCV) results in decreased numbers of packed RBC units transfused, in addition to decreased transfusion-associated complications and even decreased mortality rates. Veterinary studies investigating the use of a conservative transfusion strategy have not yet been reported. Similarly, the effect of the age and number of packed RBC units transfused has not been extensively studied in dogs.

The objective of the study reported here was to determine whether the number, volume, dose, or age of transfused packed RBC units; volume or dose of other blood products used; or pretransfusion PCV was a risk factor for transfusion-associated complications or nonsurvival in dogs. The hypothesis was that an increased number and dose of transfused packed RBC units, transfusion of older packed RBC units, administration of other blood products, and a higher pretransfusion PCV would be risk factors for transfusion-associated complications and nonsurvival.

## Materials and Methods

**Data collection**—Information was collected from the medical records of dogs that received packed RBC transfusions at the Ontario Veterinary College Health Sciences Centre between June 1, 2008, and May 31, 2011. An electronic medical record search for invoices containing the term canine packed RBCs was performed to compile the medical records from the 3-year period. The blood administration log (a handwritten workbook) was also consulted to ensure inclusion of all dogs that received documented packed RBC unit transfusions during the study time period. Dogs were excluded from analysis if the medical record or administered packed RBC unit information was incomplete or missing. Dogs that received packed RBC transfusions during > 1 visit in the study period only had information from their first visit recorded; information from subsequent visits during the study period was excluded. Dogs that previously received blood products were not excluded from analysis because this information was not consistently available in the medical record.

Information collected or calculated from each medical record and entered into a commercial spreadsheet program[a] included the signalment, body weight (kg), primary disease, APPLE score, pretransfusion PCV (%), total number and volume (mL) of packed RBC units administered, mean age (days) of packed RBC units administered, number of packed RBC units > 14 days old administered, age (days) of oldest packed RBC unit administered, volume (mL) of other (non–packed RBC) blood products (eg, FFP, platelet concentrate, or whole blood), transfusion-associated complications, and outcome. The dose (mL/kg) of blood products administered to each dog was calculated by division of the total volume (mL) of the blood product administered by the body weight (kg). The mean age of packed RBC units administered to each dog was calculated by division of the sum of the age of all packed RBC units administered by the total number of packed RBC units administered. Pretransfusion PCV was recorded as the PCV measured immediately before the packed RBC unit transfusion. If > 1 packed RBC unit was administered, only the PCV prior to the first transfusion was recorded. The APPLE (fast version) score was calculated on the basis of the most abnormal recorded blood glucose concentration, serum albumin concentration, blood lactate concentration, platelet count, and mentation score documented in the medical record during the first 24 hours of hospitalization, as reported.[23]

Transfusion-associated complications were recorded by reviewing the medical record for evidence of transfusion reactions, AKI, ALI, pneumonia, or new infections during the period between initiation of the packed RBC transfusion and death or discharge from the hospital. Transfusion reactions were considered to be any of the following as documented in the medical record during or after the packed RBC transfusions: febrile nonhemolytic reaction (rectal temperature > 39.0°C [102.2°F]); acute hemolytic reaction (hemoglobinemia, hemoglobinuria, and rectal temperature > 39.0°C); anaphylactic reaction (facial swelling, signs of pruritus, urticaria, erythema, or hypotension; systolic blood pressure < 90 mm Hg); or delayed reaction (rectal temperature > 39.0°C, unexplained decrease in PCV, or hyperbilirubinemia 5 to 10 days after transfusion).[24] Volume overload was defined as increased respiratory rate or effort or diuretic administration at the clinician's discretion during or immediately after the packed RBC transfusion. Acute kidney injury was defined as an increase in serum creatinine concentration > 1.5-fold or ≥ 0.3 mg/dL (26.4 µmol/L) from baseline or as urine output < 0.5 mL/kg/h (0.23 mL/lb/h) for 6 hours.[25] Acute lung injury was diagnosed when dogs met ALI criteria as reported.[26] Pneumonia was diagnosed when dogs had all the following: acute onset of respiratory difficulty, cough, or tachypnea; radiologic detection of pulmonary infiltrates; and hypoxemia (oxygen saturation as measured by pulse oximetry [$SpO_2$] < 95% or $PaO_2$ < 80 mm Hg) after transfusion.[27] A new infection was determined to be present if there was a positive result for a pathogen by means of microbial culture; a microorganism was detected on Gram stain of blood, urine, or other normally sterile body fluid; or an abscess or ruptured gastrointestinal tract was identified visually.

Dogs classified as surviving were alive when discharged from the hospital. Dogs were classified as nonsurviving if they were euthanized or died during hospitalization. Because of the retrospective nature of the data collection, it was not possible to discern euthanasia due to owner's financial limitations versus grave

prognosis or impending death; therefore, dogs were categorized as nonsurviving if they were euthanized or died prior to discharge.

**Blood banking protocol**—The Ontario Veterinary College Health Sciences Centre has a hospital-run canine blood-banking program that performs routine blood collections from client- and staff-owned dogs (erythrocyte antigen 1.1-positive or -negative and 1.2-positive or -negative dogs) on an as-needed basis (every 2 to 6 months) to meet the needs of hospitalized dogs requiring packed RBC transfusions. Packed RBC units were collected with a triple-bag collection system[b] and centrifuged immediately after collection for 25 minutes at 1° to 6°C at 5,000 $\times$ g. Leukoreduction filters were not used. Plasma was separated into one satellite bag and packed RBCs into another satellite bag with added RBC preservative in a closed system. All packed RBC units were labeled, sealed, and stored at 1° to 6°C for a maximum of 42 days. Blood typing of canine recipients was routinely performed to maximize use of dog erythrocyte antigen 1.1- and 1.2-positive packed RBC units. Cross-matching was also routinely performed in dogs with a history of blood product transfusion ≥ 3 days prior at the clinician's discretion. During the period of data collection, canine packed RBC units were stored in a designated refrigerator according to age (calculated as days from the date of blood collection) and size (volume in milliliters). Packed RBC units were thus categorized as ≤ 12 days old or > 12 days old and small (< 200 mL) or large (≥ 300 mL) and chosen at the discretion of the clinician or veterinary technician.

**Statistical analysis**—Descriptive statistics were performed to calculate median, range, mean, and SD for all continuous variables as well as the frequency (percentage) for transfusion-associated complications and nonsurvival (outcome). Continuous variables were analyzed for normality with a Shapiro-Wilk test. Depending on normality, a pooled Student or Wilcoxon Mann-Whitney test was used to assess differences in the mean or median for the APPLE score, pretransfusion PCV, total number of packed RBC units administered, dose of packed RBCs administered, mean age of packed RBC units administered, number of packed RBC units > 14 days old administered, age of oldest packed RBC unit administered, and dose of other blood products administered between dogs that did or did not have a documented transfusion-associated complication as well as surviving and nonsurviving dogs. Univariate exact conditional logistic regression was used to assess those same variables as risk factors for the occurrence of any transfusion-associated complication or nonsurvival. Univariate exact conditional logistic regression was also used to assess the occurrence of any transfusion-associated complication as a risk factor for nonsurvival. A multivariate best subset logistic regression approach was then used to identify risk factors for transfusion-associated complications and nonsurvival. Variables incorporated into the multivariate model included APPLE score as a measurement of illness severity as well as pertinent transfusion variables. Specifically, variables included in the multivariate analysis for transfusion-associated complications were APPLE score, number of packed RBC units administered, dose of packed RBCs administered, pretransfusion PCV, mean age of packed RBC units administered, and dose of other blood products administered. Likewise, variables included in the multivariate analysis for nonsurvival were the APPLE score, number of packed RBC units administered, dose of packed RBCs administered, pretransfusion PCV, mean age of packed RBC units administered, dose of other blood products administered, and occurrence of transfusion-associated complications. Commercially available computer software[c] was used for statistical analyses. Values of *P* < 0.05 were considered significant for all comparisons.

## Results

During the period of data collection, 243 dogs were identified as receiving packed RBC transfusions, of which 211 were included in the data analysis. Of the 32 dogs excluded from analysis, 25 had missing or incomplete medical records, and 7 had incomplete or missing information for administered packed RBC units. Of the 211 dogs included in the study, there was an equal proportion of males (103 [49%]) and females (108 [51%]), including mostly neutered males (88 [41.7%]) and spayed females (85 [40.3%]). Median age of the dogs was 7 years (range, 0.3 to 15 years), and median weight was 20.1 kg (44.2 lb; range, 1.55 to 57.0 kg [3.4 to 125.4 lb]). Mixed-breed dogs (n = 41 [19.4%]) were most commonly included, followed by Labrador Retrievers (15 [7.1%]), Cocker Spaniels (15 [7.1%]), Shih Tzus (12 [5.7%]), German Shepherd Dogs (12 [5.7%]), Golden Retrievers (12 [5.7%]), and dogs of several other breeds. Sixteen dogs had 2 visits for packed RBC transfusions during the study period; only the first visit was included.

Dogs were hospitalized for a median of 4 days (range, 1 to 24 days) for immune-mediated hemolytic anemia (n = 66 [31.3%] dogs), neoplasia (34 [16.1%]), immune-mediated thrombocytopenia (13 [6.2%]), trauma (11 [5.2%]), zinc toxicosis (5 [2.4%]), and anticoagulant rodenticide toxicosis (4 [1.9%]) most commonly. Seventy-three of the 211 (34.6%) dogs also received blood products other than packed RBC units, including FFP (54 [25.6%]), whole blood (32 [15.2%]), and platelet concentrate (14 [6.6%]). Twenty-three of 73 (31.5%) dogs that received blood products other than packed RBC units received > 1 other blood product.

Transfusion-associated complications were compared in surviving and nonsurviving dogs **(Table 1)**. One hundred eleven transfusion-associated complications occurred in 79 of the 211 (37.4%) dogs, including 19 (9.0%) dogs that had multiple transfusion-associated complications. Of these 111 transfusion-associated complications, transfusion reactions occurred most commonly (60 [54.1%]). The 60 transfusion reactions included febrile nonhemolytic reactions (n = 51 [85.0%] reactions), acute hemolytic reactions (5 [8.3%]), delayed reactions (43 [71.7%]), and anaphylactic reactions (1 [1.7%]). Others among the 111 transfusion-associated complications included AKI (n = 12 [10.8%]), new infection (11 [9.9%]), ALI (10 [9.0%]), volume overload (10 [9.0%]), and pneumonia (8 [7.2%]).

Transfusion variables in dogs that did or did not have transfusion-associated complications were summarized (**Table 2**). Of 73 dogs receiving other blood products, 37 (50.7%) developed a transfusion-associated complication, compared with 42 of 138 (30.4%) dogs that did not receive other blood products. Transfusion of other (non–packed RBC) blood products was a risk factor for transfusion-associated complications (OR, 2.35; 95% CI, 1.31 to 4.22; $P = 0.004$). Likewise, the doses (mL/kg) of packed RBCs (OR, 1.04; 95% CI, 1.01 to 1.07; $P = 0.003$) and other blood products ad-

ministered (OR, 1.04; 95% CI, 1.02 to 1.06; $P = 0.001$) were risk factors for volume overload. Multivariate logistic regression revealed that the dose (mL/kg) of other blood products administered was a risk factor for transfusion-associated complications (OR, 1.03; 95% CI, 1.01 to 1.05; $P = 0.009$).

The mortality rate was 30.8% (65/211 dogs), including 9 dogs that died and 56 dogs that were euthanized. Transfusion information for surviving and nonsurviving dogs was summarized (**Table 3**). The occurrence of a transfusion-associated complication was not a risk factor for nonsurvival ($P = 0.330$). Of 65 nonsurviving dogs, 28 (43%) had a transfusion-associated complication, compared with 51 of 146 (35%) surviving dogs. Calculation of an APPLE score was possible on the basis of available medical record information in 191 of 211 (90.5%) dogs. Higher APPLE score was a risk factor for nonsurvival (OR, 1.10; 95% CI, 1.04 to 1.17; $P < 0.001$). Multivariate logistic regression revealed that the APPLE score (OR, 1.12; 95% CI, 1.05 to 1.19; $P < 0.001$), pretransfusion PCV (OR, 1.13; 95% CI, 1.06 to 1.21; $P < 0.001$), and dose (mL/kg) of packed RBC administered (OR, 1.04; 95% CI, 1.02 to 1.07; $P = 0.001$) were risk factors for nonsurvival.

Mean age of packed RBC units, number of packed RBC units > 14 days old, and age of oldest packed RBC unit administered were not identified as risk factors for transfusion-associated complications or nonsurvival (Tables 2 and 3). Unfortunately, the study was underpowered ($\leq 27\%$ power) to detect age of packed RBC units as a significant risk factor for transfusion-associated complications or nonsurvival given that only approximately one-fourth of dogs received packed RBC units, with a mean packed RBC unit age > 14 days

Table 1—Number (%) of transfusion-associated complications in 211 dogs that received a packed RBC transfusion and did (n = 146) or did not (65) survive.

| Complication | Surviving dogs | Nonsurviving dogs | P value |
|---|---|---|---|
| Febrile reaction | 37 (25.3) | 14 (21.5) | 0.681 |
| Acute hemolytic reaction | 4 (2.7) | 1 (1.5) | 1.000 |
| Anaphylactic reaction | 1 (0.7) | 0 (0) | 1.000 |
| Delayed reaction | 3 (2.1) | 0 (0) | 0.658 |
| Volume overload | 2 (1.4) | 8 (12.3) | 0.003 |
| | | | |
| AKI | 4 (2.7) | 8 (12.3) | 0.011 |
| Stage 1 | 2 (1.4) | 3 (4.6) | |
| Stage 2 | 1 (0.7) | 3 (4.6) | |
| Stage 3 | 1 (0.7) | 2 (3.1) | |
| Pneumonia | 2 (1.4) | 6 (9.2) | 0.023 |
| New infection | 6 (4.1) | 5 (7.7) | 0.287 |
| ALI | 3 (2.1) | 7 (10.8) | 0.029 |

Surviving dogs were dogs that were discharged from the hospital alive, and nonsurviving dogs were dogs that died or were euthanized while hospitalized. Febrile was defined as rectal temperature > 39.0°C (102.2°F). Nineteen dogs had > 1 transfusion-associated complication and are represented in each category they were affected.

Table 2—Clinical and transfusion information for 211 dogs that received a packed RBC transfusion and subsequently did (n = 79) or did not (132) develop transfusion-associated complications.

| Variable | Dogs with transfusion-associated complications | Dogs without transfusion-associated complications | P value |
|---|---|---|---|
| APPLE score | 25.1 ± 5.9 | 24.8 ± 5.9 | 0.799 |
| Pretransfusion PCV (%) | 17.7 (8–52) | 16 (7–46) | 0.248 |
| No. of packed RBC units administered | 1 (1–4) | 1 (1–6) | 0.213 |
| Dose of packed RBCs administered (mL/kg) | 14.4 (5.4–94.7) | 12.9 (0.9–76.4) | 0.112 |
| Mean age of packed RBC units administered (d) | 7 (0–40) | 8 (0–34) | 0.636 |
| No. of packed RBC units > 14 days old administered | 0 (0–3) | 0 (0–4) | 0.397 |
| Age of the oldest packed RBC unit administered (d) | 9 (0–40) | 9 (0–34) | 0.614 |
| Dose of other blood products administered (mL/kg) | 0 (0–99.4) | 0 (0–106.8) | 0.003 |

Values are reported as mean ± SD or median (range).

Table 3—Clinical and transfusion information for 211 hospitalized dogs that received packed RBC transfusions and did (n = 146) or did not (65) survive.

| Variable | Surviving dogs | Nonsurviving dogs | P value |
|---|---|---|---|
| APPLE score | 24.0 ± 5.6 | 27.1 ± 6.0 | < 0.001 |
| Pretransfusion PCV (%) | 16 (7–46) | 18 (9–52) | 0.015 |
| No. of packed RBC units administered | 1 (1–4) | 1 (1–6) | 0.092 |
| Dose of packed RBCs administered (mL/kg) | 13.2 (0.9–70.8) | 14.4 (1.9–94.7) | 0.527 |
| Mean age of packed RBC units administered (d) | 7.5 (0–40) | 8 (0–34) | 0.567 |
| No. of packed RBC units > 14 days old administered | 0 (0–3) | 0 (0–4) | 0.886 |
| Age of the oldest packed RBC unit administered (d) | 8 (0–40) | 9 (0–34) | 0.319 |
| Dose of other blood products administered (mL/kg) | 0 (0–78.6) | 0 (0–106.8) | 0.017 |

*See* Tables 1 and 2 for key.

(48/211 [22.7%]) or ≥ 1 packed RBC unit > 14 days old (55/211 [26.1%]).

## Discussion

In the present study, transfusion-associated complications occurred in 37% of dogs, with an overall incidence of transfusion reactions of approximately 28%. The incidence of transfusion reactions in the present study was higher than reported in studies performed in dogs 15 to 20 years ago,[1,2] but was still less than that reported for dogs that received a massive transfusion.[3] Given the increased awareness of the complications of packed RBC transfusions, clinicians are likely more diligent in monitoring for and recording transfusion reactions, which might account for the increased incidence in the present study. The overall reported incidence of other transfusion-associated complications in the present study was also higher than that reported in the human literature, with studies[12,13,21] investigating morbidity associated with packed RBC transfusions revealing an overall transfusion-associated complication rate of approximately 7% to 18%. However, circulatory overload, which accounted for 9% of the transfusion-associated complications in the present study, is not always recorded as a transfusion-associated complication in human studies and therefore likely increased the incidence of transfusion-associated complications in the present study. Additionally, the use of leukoreduction in human blood banks has decreased the rate of transfusion-associated complications in humans receiving packed RBC transfusions,[28] and considering that dogs in the present study received packed RBC units containing leukocytes and platelets, we would expect their complication rate to be higher. In 2 studies[13,21] investigating pediatric and adult cardiac surgery patients receiving packed RBC transfusions, the incidence of AKI was 2.5% and 2.1%, the incidence of pulmonary complications or pneumonia was 7.7% and 3.2%, and the incidence of other infectious complications was 3.2% and 6.0%, respectively. The present study revealed fairly similar findings: the overall incidence of AKI was 5.7%, the overall incidence of pneumonia was 3.8%, and the overall incidence of new infection was 5.2%.

The present study also revealed that transfusion of other (non–packed RBC) blood products was a risk factor for transfusion-associated complications; for every other blood product transfusion, the risk of transfusion-associated complications increased almost 3-fold. Likewise, multivariate analysis revealed that the dose (mL/kg) of other blood products transfused was a risk factor for transfusion-associated complications. Non–packed RBC units transfused included whole blood, FFP, or platelet concentrate, which all contain a larger quantity of plasma and therefore protein than does a packed RBC unit and thus have a greater propensity for causing immunologic reactions unrelated to RBC incompatabilities.[28] Most of the recent human literature investigating transfusion-associated complications is focused on the incidence and pathogenesis of ALI, specifically transfusion-related ALI that occurs within 6 hours after a transfusion.[29–31] Studies[29,31,32] in humans indicate that the risk of transfusion-related ALI is great-

er in patients who receive plasma-rich blood products, FFP, or platelets, compared with those patients who receive packed RBC units only, especially when those non–packed RBC products are collected from women with a history of pregnancy. Although transfusion-related ALI has been reviewed in the veterinary literature[33] and massive transfusion is considered a risk factor for ALI,[26] there are no published case reports of transfusion-related ALI in veterinary patients, to our knowledge. As such, it is unlikely that transfusion-related ALI occurs in veterinary recipients, especially given that most veterinary blood donors are spayed or neutered. Therefore, although the present study retrospectively revealed evidence of ALI in dogs after administration of packed RBC transfusions, whether ALI was related to the transfusion itself or an underlying disease that could also predispose to ALI was unknown.

Volume overload occurred in approximately 9% of dogs with transfusion-associated complications in the present study (approx 5% of dogs overall), and the dose (mL/kg) of packed RBCs and other blood products was a risk factor. Volume overload or transfusion-associated circulatory overload occurs in approximately 6% of human medical intensive care patients who receive blood transfusions,[34] similar to the incidence reported in the present study. Additionally, FFP transfusion is a risk factor for transfusion-associated circulator overload in humans,[34–36] which is also consistent with the finding of increased transfusion-associated complications in dogs in the present study that received non–packed RBC blood products, the majority (74%) of which received FFP.

After accounting for disease severity by incorporating APPLE scores into a multivariate statistical analysis, pretransfusion PCV and dose (mL/kg) of packed RBCs administered were significant risk factors for nonsurvival in the present study. The number of packed RBC units transfused has long been associated with increased mortality rate in human patients,[18,21] but this relationship was not found in a previous study[2] in dogs. However, in dogs with anemia caused by ineffective erythropoiesis, the pretransfusion PCV was significantly higher in the dogs that did not survive.[2] Findings of the present study also suggested that use of a higher pretransfusion PCV to trigger the administration of packed RBC units, thereby administering a larger total dose of packed RBCs than would otherwise be given with a more conservative transfusion trigger, was associated with increased risk of nonsurvival. Certainly, recent studies[7,8,22] in human medicine consistently support the use of conservative transfusion strategies for several critically ill patient populations. Recent recommendations from the American Association of Blood Banks suggest adherence to a restrictive transfusion strategy, triggered at a hemoglobin concentration of 7 to 8 g/dL (approximate pretransfusion PCV, 21% to 24%) in stable hospitalized patients, and use of the higher end of the hemoglobin transfusion trigger for patients with symptoms of anemia or preexisting cardiovascular disease.[37] The median pretransfusion PCV was lower than this suggested trigger in both surviving and nonsurviving dogs in the present study but had a wide range across the studied population. A prospective investiga-

tion of the use of a conservative transfusion trigger in veterinary patients is warranted to determine whether a conservative transfusion strategy would reduce rates of death or transfusion-associated complications in dogs that require packed RBC transfusions.

In the present study, transfusion-associated complications were not identified as a risk factor for nonsurvival. To the authors' knowledge, risk factors for transfusion-related complications and the association of these complications with outcome have not been previously reported in dogs. In humans, transfusion-related complications, encompassing both immunologic and nonimmunologic reactions, are extensively discussed in the literature because of their effect on patient comfort and mortality rate.[28,38] The 3 most common causes of transfusion-related deaths in humans include transfusion-related ALI, transfusion-associated circulatory overload, and hemolytic transfusion reactions, in that order.[38] Acute lung injury, volume overload, and hemolytic reactions were all reported in the dogs that received packed RBC transfusions in the present study. Unfortunately, given the retrospective nature of the study and the limitations of interpreting information from the medical record, it was impossible to confirm whether these complications occurred because of the transfusion and resulted in the dog's death.

Dose of packed RBC units administered and higher pretransfusion PCV were identified as risk factors for nonsurvival; however, the mean age of packed RBC units, number of packed RBC units > 14 days old, and age of oldest packed RBC unit administered were not. Unfortunately, the present study was statistically underpowered to detect significant associations with packed RBC age, given the disparate number of dogs that received packed RBC units > 14 days old, compared with dogs that received units < 14 days old. A number of recent studies[12–17] reveal that transfusion of packed RBC units stored for greater durations leads to increased morbidity and mortality rates in human patients. Experimental studies[d,e] also reveal that dogs that receive a transfusion with 35-day-old packed RBC units develop leukocyte changes, thrombocytopenia, marked hypocoagulability, more hemolysis, and a greater inflammatory response, compared with dogs transfused with 3-day-old packed RBC units. Likewise, a recent experimental study[39] involved the use Beagles with induced staphylococcal pneumonia and sepsis that received a transfusion of 80 mL/kg (36.4 mL/lb; in 4 divided doses) of either 42-day-old or 7-day-old blood. Dogs that received the older stored blood had greater mortality rates as well as greater frequency of lung injury at the site of infection on postmortem examination.[39] The findings in that study[39] were likely exaggerated by the large difference in the age of the packed RBCs administered. Conversely, in the present study, none of the dogs received blood > 40 days old, and few dogs received blood > 21 days old. This was likely because of the division of stored packed RBC units according to age at the Ontario Veterinary College Health Sciences Centre and the subsequent preference for transfusing newer packed RBC units. A larger study including hospitals that have a greater propensity to administer older packed RBC units would be ideal to investigate the issue of the effect of age of packed RBC units on morbidity and mortality rates in dogs. Unfortunately, such studies are difficult to design,[40,41] and as such, definitive results from prospective human studies investigating the age of packed RBC units on outcome are still lacking.

Limitations of the present study that warrant discussion are related to its retrospective design and limited statistical power. This design inherently had biases that could have negatively affected the strength of the findings, particularly the selection bias and information bias (misclassification) that are inherent in retrospective studies. Specifically, even though one author was responsible for collection and interpretation of data from the medical records, there was still reliance on others for accurate record keeping. Thus, the incidence of transfusion-associated complications might have been misrepresented. This was especially possible with regard to transfusion-associated complications that were subjectively diagnosed on the basis of a documented clinical impression, such as transfusion-associated circulator overload. Likewise, it was difficult to retrospectively discern an acute hemolytic reaction from clinical manifestations of the underlying disease, as in dogs with immune-mediated hemolytic anemia. Most importantly, it was impossible to determine cause and effect in terms of the relationship between transfusion variables and transfusion-associated complications or nonsurvival. In other words, dogs that had transfusion-associated complications or died could have done so simply because of progression of the underlying disease or critical illness, rather than the transfusion variables themselves. Many of the transfusion-associated complications, including AKI or ALI, occur relatively commonly in critically ill patients, independent of blood product administration. Therefore, although the APPLE score was incorporated into the statistical analysis to account for an association between the severity of illness and transfusion-associated complications or nonsurvival, lack of an association between the APPLE score and transfusion variables did not rule out progression of critical illness as a cause of the transfusion-associated complications.

Unfortunately, the study was underpowered to adequately detect an association between the age of packed RBC units administered and transfusion-associated complications or outcome, given that older blood is infrequently administered at this hospital and is administered at the discretion of the attending clinician. Also, the present study included a heterogeneous group of dogs with many underlying conditions and requirements for packed RBC transfusions, which also precluded drawing firm conclusions regarding the effect of transfusion variables on transfusion-associated complications and nonsurvival. Likewise, previous transfusion history, blood type compatibility, and crossmatch results were not taken into consideration and might also have been associated with the incidence of transfusion-associated complications. Prospective studies are needed to determine the associations between conservative and liberal transfusion triggers as well as the age of stored packed RBC units and transfusion-associated complications and mortality rate in dogs.

Transfusion-associated complications occurred in 37% of dogs that received packed RBC transfusions,

and dogs administered other blood products were at a higher risk. This finding supports the rigorous monitoring of dogs during and after packed RBC transfusions for transfusion-associated complications, especially in dogs administered non–packed RBC blood products. The dose (mL/kg) of packed RBC units transfused and a higher pretransfusion PCV were risk factors for non-survival regardless of illness severity, suggesting a potential benefit of a conservative transfusion strategy in dogs.

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