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Retrospective Evaluation of Risk Factors and Outcome in Dogs With and Without Fluid Overload During Hospitalization

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ABSTRACT

Background: Risk factors for the development of fluid overload (FO) and its potential negative effects have not been investigated in dogs.

Hypothesis/Objectives: Evaluate risk factors and outcomes in hospitalized dogs that received fluids IV and developed clinical signs of FO compared to those that did not.

Animals: One hundred thirty-six dogs that developed FO and 109 dogs without FO.

Methods: Retrospective observational study of hospitalized dogs. Variables were compared between dogs that developed clinical signs of FO (FO group) and dogs without FO (control group).

Results: Compared to the control group, dogs in the FO group were significantly more likely to have cardiovascular disease (odds ratio [OR], 18.1; 95% confidence interval [CI], 5.4–60), protein-losing nephropathy (OR, 15.3; 95% CI, 2.0–116.8), chronic kidney disease (OR, 10; 95% CI, 3.0–33.8), and acute kidney injury (OR, 5.2; 95% CI, 2.5–10.6). The total fluid volume administered IV was not significantly different between the groups ($p = 0.16$). Only 6.0% of dogs with clinical signs of FO gained > 10% weight from non-dehydrated baseline and thus met the FO definition used in human medicine. Compared with the control group, dogs with FO had a significantly longer median duration of hospitalization ($p < 0.001$) and were less likely to survive to discharge ($p < 0.001$).

Conclusions and Clinical Importance: FO was more common with certain underlying diseases but not associated with total fluid volume administered IV. The definition for FO in human medicine using weight gain requires further evaluation in dogs. FO was associated with worse outcomes and longer hospitalization time.

Abbreviations: AKI, acute kidney injury; APPLE, Acute Patient Physiologic and Laboratory Evaluation; BCS, body condition score; CKD, chronic kidney disease; FO, fluid overload; ICU, intensive care unit; IV, intravenously; IVAF, intravenous administration of fluids; LRS, lactated Ringer's solution; PLN, protein losing nephropathy.

1 | Introduction

Fluid therapy plays a critical role in the treatment plan of most hospitalized humans, dogs, and cats [1, 2]. The IV administration of fluids (IVAF) is used to increase cardiac output and enhance tissue oxygen delivery during resuscitation, replace fluid deficits, and maintain total body water and electrolyte balance [3, 4]. Optimal fluid therapy is impacted by a variety of factors, including the indication for treatment, underlying disease processes, and severity of illness [1, 5–8].

Despite its benefit, IVAF is not without potential negative effects. In people, a positive fluid balance, defined as fluid gain higher than fluid loss, helps prevent microcirculatory collapse and organ failure during the early phase of hospitalization and resuscitation [6, 9, 10]. However, progressive positive fluid balance after achieving hemodynamic stabilization and adequate hydration can lead to fluid overload (FO) [1, 11–15]. In human medicine, FO is commonly defined as the "expansion of extracellular fluid volume with a positive fluid balance that produces a weight gain > 10% from non-dehydrated baseline," [16–18] and has been associated with longer hospitalization, increased need for mechanical ventilation, acute kidney injury (AKI), abdominal compartment syndrome, organ dysfunction, and up to 70% increased mortality [1, 6, 7, 19].

Fluid overload affects more than 25% of human patients in the intensive care unit (ICU) [18]. Human patients with AKI, acute lung injury, and septic shock are especially susceptible to the development and the effects of FO [11–14]. Multiple studies in people have demonstrated an association between FO and mortality [1, 6, 20–22]. For example, a recent study in people demonstrated that every additional 1 L of positive fluid balance increased the risk of death by up to 6% [20]. Risk factors for the development of FO and its potential negative effects have not been reported in dogs. This information could help optimize fluid therapy management in dogs.

Our objective was to retrospectively evaluate potential risk factors, hospitalization time, and outcome in hospitalized dogs receiving IVAF that developed clinical signs of FO compared to those without FO. We hypothesized that dogs that developed FO during hospitalization would have risk factors (e.g., underlying disease process, fluid volume administered) and worse outcomes compared with dogs that did not develop FO.

2 | Materials and Methods

2.1 | Case Selection Criteria

All cases were selected from the electronic medical record system of our veterinary teaching hospital using a computer-based query followed by manual review. FO was defined as the development of peripheral edema, respiratory signs (e.g., tachypnea, dyspnea), pulmonary edema, or body cavity effusion while receiving IVAF, and the signs were attributed to FO by the clinician.

To generate a pool of potentially eligible dogs that developed FO as well as controls without FO, the electronic medical record system was searched for dogs hospitalized through any service between January 1, 2020 and December 31, 2020. The computer query included dogs that were hospitalized for a minimum of 3 consecutive days, received IVAF, had body weights recorded daily for at least the first 3 days of hospitalization, and had blood test results recorded at admission and at least one additional time point during hospitalization.

Our 1-year search identified 714 potentially eligible dogs that met the query criteria. Medical records from these potentially eligible dogs were reviewed in chronological order by one of four veterinary students. Dogs that did not meet all of the inclusion criteria, dogs that already had FO at the time of admission (i.e., before IVAF), and dogs with incomplete medical records that prohibited completion of the data collection sheet were excluded (Figure 1). After reviewing medical records for 280 dogs admitted from January 1, 2020 to June 15, 2020, 143 dogs were excluded, leaving 137 controls and three dogs with FO that appeared to meet all of the inclusion and exclusion criteria. Given the small number of dogs with FO identified (3/280 or 1%) during the recording of data for the control group, a second data query was performed to identify dogs with FO by extending the searched dates from July 1, 2015 to December 31, 2020. As with the initial query, this second query included dogs that were hospitalized for a minimum of 3 consecutive days, received IVAF, had body weights recorded daily for at least the first 3 days of hospitalization, and had blood test results recorded at admission and at least one additional time point during hospitalization. However, for this second query, a clinician assessment including any mention of FO in the medical records was added. Dogs with FO identified from this second search then were compared to control dogs identified from the initial search (Figure 1).

2.2 | Medical Records Review

Data were recorded for all dogs during the first 3 days of hospitalization. For dogs with extended hospitalization (> 3 days), data were recorded for a maximum of 5 days. Data were not recorded beyond 5 days of hospitalization because of the relatively small numbers of dogs with hospitalization times > 5 days. Data collected included baseline characteristics (age, sex, breed, body weight, body condition score [BCS]) and the Acute Patient Physiologic and Laboratory Evaluation (APPLE)fast score as recorded on admission [23].

Disease categories were classified as follows: sepsis, trauma, chronic kidney disease (CKD), AKI, protein-losing nephropathy (PLN), cardiovascular disease, surgery/soft tissue, surgery/orthopedic, neoplasia, respiratory, neurologic, gastrointestinal (chronic gastrointestinal disease, acute vomiting, diarrhea, regurgitation, pancreatitis, liver disease), endocrine, and metabolic (severe electrolyte abnormalities, toxin ingestion, autoimmune disease). Disease categories were assigned to dogs based on clinical diagnoses described in the medical record. Dogs could be assigned to multiple disease categories if applicable.

The highest daily body weight, volume of IVAF per day, and total volume of IVAF during hospitalization were recorded for

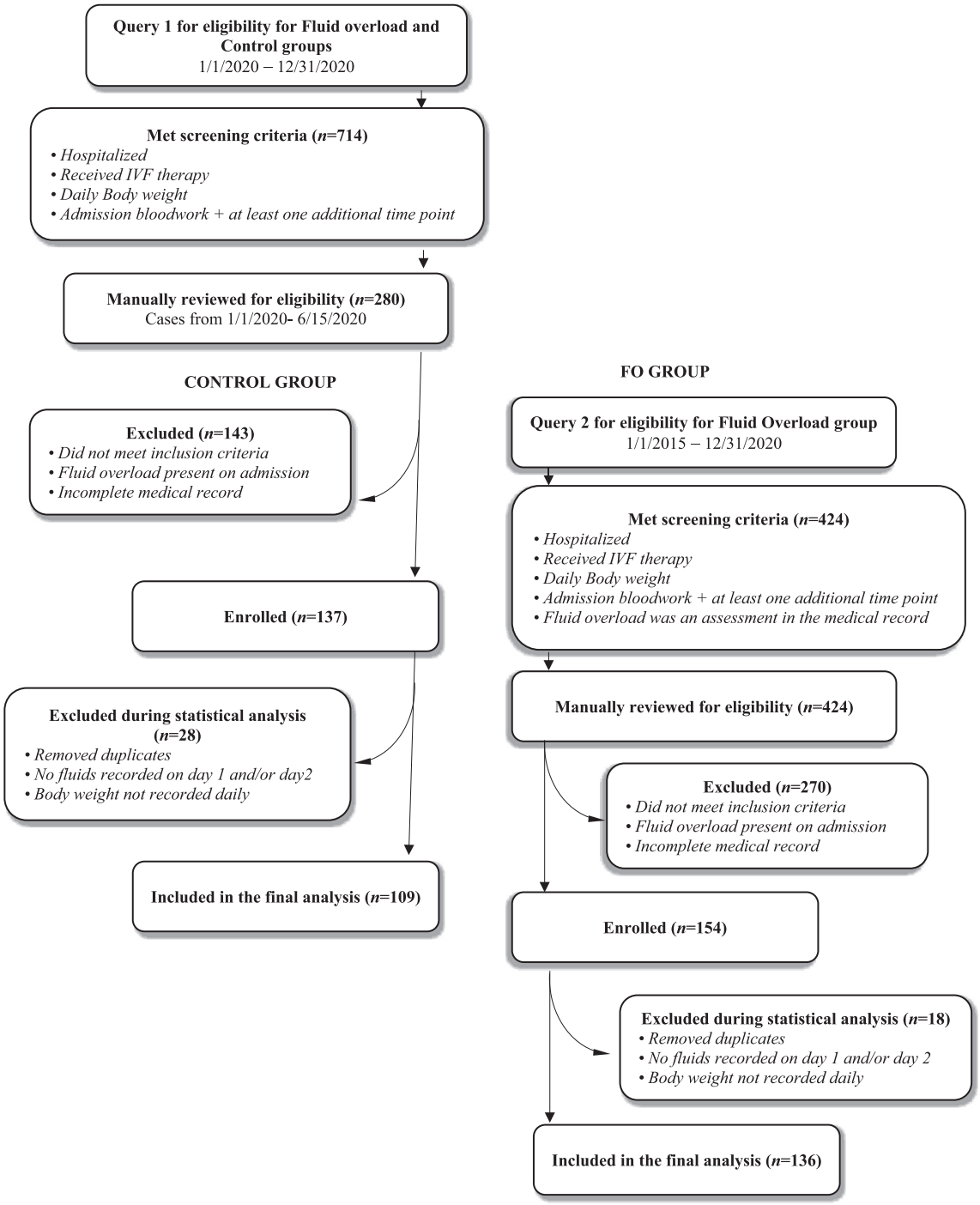

FIGURE 1 | CONSORT diagram showing the flow of record screening, enrollment, and exclusion during statistical analysis to determine dogs that were included in the final analysis of dogs with and without fluid overload.

up to 5 days of hospitalization. Fluid volumes were determined by summarizing 24 h volumes of fluids recorded in the medical record and included all types (i.e., crystalloids, blood transfusions, albumin, synthetic colloids) and doses, such as boluses, volume during anesthetic procedures, continuous rate infusions (CRIs), diluted medications, replacement and maintenance fluids as well as enteral nutrition, received by each dog for up to 5 days of hospitalization. Enteral water and parenteral nutrition as well as fluid losses were only available and quantified for a small subset of dogs and therefore were not included in the analysis. Volumes of fluid administered to maintain IV catheter patency also were not included because they are not typically recorded at our institution.

A non-dehydrated baseline body weight was calculated using the following formula, based on the first body weight recorded and the clinician's percent dehydration assessment at the time of admission (%): body weight at admission in kg + (body weight at admission in kg × percent dehydration)/100. To compare our results to the definition of FO used in human medicine [16–18] (but not the definition for FO for our study), the number of dogs with weight gain > 10% from non-dehydrated baseline body weight was recorded.

Finally, the total duration of hospitalization, whether dogs were hospitalized in the ICU, the total cost of treatment, and the outcome were recorded. The outcome was categorized as survival to discharge, death before discharge, or euthanasia before discharge.

2.3 | Statistical Analysis

Data distributions were examined using the Shapiro–Wilk test. Continuous variables are presented as mean ± SD for normally distributed variables or median (interquartile range [IQR]) for skewed variables. Categorical variables are reported as frequency (percentage). The FO and control groups were compared using independent sample *t*-tests for normally distributed continuous variables, Wilcoxon rank sum tests for skewed continuous variables, and chi-squared tests for categorical variables. Fisher's exact tests were used for categorical variables with expected cell counts < 5. Multiple regression models were developed, adjusting for confounders (age, sex, fluid volume) without changes in the effect size. Given the lack of a confounding association, the unadjusted data were used for our study. For variables with longitudinal data from Days 1 to 5 (weight and fluid volume variables), a linear mixed effects model was used to determine if the mean response varied between the FO and control groups. The FO group was set as the fixed effect in the model, whereas the random effect models the within-subject (dog) variability for the repeated measures, using a restricted maximum likelihood estimation. This modeling used the lmer4 package in RStudio [24].

Odds ratios (ORs) and 95% confidence intervals (CIs) for comparison between groups are reported as effect measures from logistic regression analyses. $p < 0.05$ were deemed statistically significant. RStudio was used for all statistical analyses (R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/).

3 | Results

An automated data query retrieved 714 records of dogs hospitalized in 2020 that met the query criteria for the study. Of the first 280 medical records manually reviewed, 143 were excluded based on predefined inclusion and exclusion criteria or because of incomplete records, leaving 137 dogs without FO that met all inclusion criteria for the control group. During the statistical analysis, an additional 28 dogs had to be excluded because of incomplete medical records, leaving 109 dogs in the control group that were included in the final analysis (Figure 1).

From the initial medical records query, only three dogs that met all of the query criteria also met the inclusion criteria for the FO group. Therefore, a second data query was performed that identified 424 dogs that met the query criteria and underwent a manual review of medical records. After excluding 270 cases that did not meet inclusion criteria or had incomplete data, 154 cases were included in the FO group. Eighteen additional dogs had to be excluded during statistical analysis because of incomplete medical records, leaving 136 dogs in the FO group that were included in the final analysis (Figure 1). After the analysis of 280 records for dogs in the control group, as well as the records for the FO group, funding did not allow for the student assistants to review time-matched records for dogs in the control group to incorporate the same time frame as the FO group.

Although the number of FO cases per year was relatively consistent across the first 5 years (7 dogs with FO in 2015, 16 dogs in 2016, 22 dogs in 2017, 13 dogs in 2018, 18 dogs in 2019), the largest number of cases was enrolled in 2020 (60/137). Of those 60 cases, 43 were admitted during the second half of 2020, whereas the control group included cases from the first half of 2020.

No significant differences were found between groups in age, sex, body weight at admission, BCS, or APPLEfast score on admission (Table 1). More dogs in the FO group (76.5%) were hospitalized in the ICU compared with the control group (58.7%; $p = 0.003$; Table 1).

Dogs in the FO group were significantly more likely to have cardiovascular disease (OR, 18.1; $p < 0.001$). Dogs in the FO group also were 15.3, 10.0, and 5.2 times more likely to have PLN, CKD, or AKI, respectively (Table 2). They also were more likely to be categorized as having metabolic disease (OR, 4.9; $p < 0.001$), gastrointestinal disease (OR, 3.0; $p < 0.001$), and respiratory disease (OR, 3.2; $p = 0.002$; Table 2). Dogs in the FO group were significantly less likely to have trauma (OR, 0.2; $p = 0.004$) or soft tissue surgery (OR, 0.3; $p \leq 0.001$; Table 2). Adjustment for volume of IVAF did not change these results (data not shown).

No difference was found in the volume of IVAF per day or the total volume of IVAF from Days 1 to 5 between the FO and control groups (total mL or mL/kg; Table 1).

Over the course of hospitalization (up to Day 5), median percent body weight increased on each day for dogs in the FO group (2.4% Day 2, 2.8% Day 3, 3% Day 4, and 2.5% Day 5), and was static or decreased in the control group (0% Day 2 [$p < 0.001$], 0% Day 3 [$p < 0.001$], −0.8% Day 4 [$p < 0.001$], and −1.7% Day 5 [$p < 0.001$]; Table 1). Dehydration assessment was not available for 20 dogs in the FO group and four dogs in the control group. Therefore, non-dehydrated baseline weight only could be calculated for 116 dogs in the FO group and 105 dogs in the control group. No difference was found in the percentage of dogs that gained at least 10% of their non-dehydrated baseline weight between the groups (FO group: 7/116 [6.0%] vs. control group: 3/105 [2.9%]; $p = 0.34$; Table 1). The three dogs in the control group that gained at least 10% of their non-dehydrated baseline weight had no clinical signs of FO as specified by the study's exclusion criteria.

Median duration of hospitalization was significantly longer for the FO group (6 days; IQR, 5–9 days) compared with the control group (5 days; IQR, 4–7 days; $p < 0.001$; Table 1). Dogs in the FO group were significantly less likely to survive to discharge (68.4%) compared with the control group (92.7%; $p \leq 0.001$; Table 1). More dogs were euthanized in the FO group (37/43 [86.1%]) compared with the control group (1/8 [12.5%]). Median cost of hospitalization was significantly higher in the FO group ($5760; IQR, $4084–8873) compared with the control group ($5401; IQR, $3739–6685; $p = 0.02$; Table 1).

TABLE 1 | Baseline characteristics, fluid volumes, body weight and weight changes, and outcome for hospitalized dogs that received intravenous fluids that developed or did not develop fluid overload. Data are presented as median (interquartile range) or frequency (percent). The total number of dogs for each variable is indicated if not all dogs in that group had the information available.

	Fluid overload group ($n=136$)	Control group ($n=109$)	p	Effect size (95% CI)
Baseline characteristics				
Age (years)	9 (5–11)	7 (5–10)	0.38	0 (−2, 1)
Sex				
Male	68 (50.0%)	64 (58.7%)	0.17	0.7 (0.4, 1.2)
Female	68 (50.0%)	45 (41.3%)		
Body condition score (1–9)	5 (5–6) $n=135$	6 (5–7) $n=108$	0.17	0 (0, 1)
APPLEfast at admission	21.5 (18.8–26.0) $n=90$	19 (15–22) $n=47$	0.09	3 (1, 5)
Hospitalization				
Days in hospital	6 (5–9)	5 (4–7)	< 0.001	1 (1, 2)
Hospitalized in the intensive care unit	104 (76.5%)	64 (58.7%)	0.003	2.3 (1.3, 4.0)
Outcome				
Survived to discharge	93 (68.4%)	101 (92.7%)	< 0.001	0.17 (0.1, 0.4)
Cause of death			1	1.14 (0.1, 10.9)
Euthanasia	37/43 (86.0%)	1/8 (12.5%)		
Natural death	6/43 (14.0%)	7/8 (87.5%)		
Cost of hospitalization ($)	5760 (4084–8873)	5401 (3739–6685)	0.02	817 (131, 1493)
Body weight				
Non-dehydrated baseline weight (kg)	21.6 (9.0–34.2) $n=118$	12.9 (6.8–28.6)	0.08	2.7 (−0.4, 6.4)
Percent change in weight from Day 1 to Day 2	2.4 (0.0–4.8)	0.0 (−1.2 to 3.0)	< 0.001	1.7 (0.8, 2.7)
Percent change in weight from Day 1 to Day 3	2.8 (0.0–6.6)	0.0 (−2.3 to 3.4)	< 0.001	2.5 (1.2, 0.37)
Percent change in weight from Day 1 to Day 4	3.0 (−1.3–7.9) $n=119$	−0.8 (−3.7 to 2.3) $n=107$	< 0.001	3.9 (2.3, 5.6)
Percent change in weight from Day 1 to Day 5	2.5 (−1.6–6.1) $n=104$	−1.7 (−4.5 to 1.2) $n=73$	< 0.001	4.2 (2.5, 5.7)
Weight gain > 10% during hospitalization (from non-dehydrated baseline weight)	7 (6.0%) $n=116$	3 (2.9%) $n=105$	0.34	2.18 (0.48, 13.39)
Intravenous fluid volumes				
Day 1 (mL)	303 (122–731)	254 (100–507)	0.09	67 (−3, 149)
Day 2 (mL)	1186 (466–2168)	799 (472–1778)	0.11	169 (−36, 410)
Day 3 (mL)	861 (360–1725)	764 (439–1621)	0.98	2 (−187, 194)
Day 4 (mL)	714 (201–1613)	583 (289–1286)	0.94	0 (−156, 187)
Day 5 (mL)	383 (0–1467)	224 (0–669)	0.08	16 (0, 210)

(Continues)

TABLE 1 | (Continued)

	Fluid overload group ($n = 136$)	Control group ($n = 109$)	p	Effect size (95% CI)
Total fluid volume Day 1–5 (mL)	3989 (1629–7610)	2782 (1539–5861)	0.16	497 (−173, 1315)
Total fluid volume Day 1–5 (mL/kg)	222 (141–310) ($n = 118$)	224 (161–296)	0.92	2 (−32, 29)

4 | Discussion

In our retrospective study of hospitalized dogs that received IVAF, FO was associated with a lower likelihood of survival to discharge. Although a causal relationship cannot be identified by a retrospective study, these findings are consistent with results of another retrospective study of 34 critically ill dogs that also identified an association between FO and a higher risk of death [25]. Fluid overload also was associated with a longer median hospitalization time and increased cost of hospitalization in the dogs in this study [25]. Similarly, in a study of 11 cats with urethral obstruction, FO was associated with higher costs and a longer duration of hospitalization but was not associated with higher mortality [26]. In human patients, FO was associated with approximately 1.5 times higher hospitalization costs and ICU costs were nearly two times higher [12, 27]. In our study, the APPLEfast score at the time of admission was not significantly different between the groups, whereas critically ill people that develop FO had higher injury severity scores [28, 29]. Evaluation of changes in APPLEfast scores over the course of hospitalization was not possible in our patient population because of missing data points but would be interesting to evaluate in future studies. The differences in these outcomes in dogs included in our study might not be exclusively associated with the development of FO, and other factors could be contributory. The higher mortality rate in the FO group, for example, could be attributed to the higher prevalence of certain disease conditions, such as cardiovascular or respiratory diseases, which were more common in the FO group.

Anecdotally, dogs and cats with heart disease, CKD, hypoalbuminemia, or vasculitis secondary to sepsis or systemic inflammatory response syndrome appear to be predisposed to the development of FO [30, 31]. In people, multiple studies confirmed that patients with AKI, acute lung injury, and septic shock seem to be especially sensitive to the development and effects of FO [11–14, 18–21]. In our study, dogs in the FO group were significantly more likely to be categorized as having cardiovascular disease. Many human patients with chronic congestive heart failure develop intravascular and interstitial fluid volume expansion because of renal retention of sodium and water [32], which increases the risk of developing FO when challenged with IVAF [33, 34].

Dogs in the FO group also were more likely to be categorized in one of the three categories of renal dysfunction (i.e., PLN, CKD, AKI). The reason for this result might be multifactorial. Dogs and cats with CKD and AKI often initially are treated with large doses of fluids administered IV to optimize intravascular circulating volume and improve renal blood flow, oxygen supply, and glomerular filtration rate (GFR), because hypotension can be detrimental to renal function [35]. Concurrently, animals and people with CKD can have marked derangements in their ability to regulate fluid homeostasis [35, 36]. Animals with AKI frequently are oliguric because of an impaired ability to excrete excess fluid, which can increase their risk for FO [37].

Dogs in the FO group were significantly less likely to have trauma or soft tissue surgery. People with severe trauma and hemorrhagic shock are considered at increased risk for FO because of aggressive fluid resuscitation [38]. The contrary finding in our population of dogs might indicate that many of the cases only had mild to moderate trauma without massive hemorrhage and resuscitation needs. Low occurrence of trauma in both groups might be another explanation. Similarly, many of the dogs in the soft tissue group included stable foreign body surgeries without major systemic inflammation or large fluid needs.

As described above, sepsis is a well-established risk factor for FO in people [18–22]. Although the OR for sepsis in our study was not significant, this result could have been related to the relatively small sample size and low prevalence of sepsis (8.0% in the FO group, 3.7% in the control group).

The volume of IVAF (total mL or mL/kg) was not different between the groups for any day. This finding suggests that the development of FO is not simply a consequence of the total fluid volume administered. In an experimental study in mildly dehydrated dogs, administration of large volumes of lactated Ringer's solution (LRS) in 1 h did not result in the development of FO [39].

In recent years, fluids administered as drug diluents, with enteral nutrition and to maintain catheter patency have been emphasized in the human medical literature as "hidden fluids" that are not accounted for in fluid plans and calculations [40]. They might account for up to 61% of total daily fluid intake in people and have been correlated with FO and increased duration of hospitalization [40–43]. Although the fluid volume calculations in our study included the majority of hidden fluids such as enteral nutrition, medication dilution, and CRIs, others were not included (e.g., enteral water, IV catheter irrigations). This factor might have resulted in underestimation of the total fluid volumes administered in both groups, and therefore represents a limitation of our study.

Another limitation is derived from the lack of one universally accepted definition for FO. In dogs and cats, FO often is a clinical diagnosis [30, 31]. In our study, FO was defined as the development of peripheral edema, respiratory signs (if attributed to FO), or body cavity effusion. This definition is subjective, and different clinicians might interpret clinical signs differently. As a result, some dogs could have been misdiagnosed with FO or subclinical signs of FO, such as chemosis or nasal discharge,

TABLE 2 | Comparison of disease categories for hospitalized dogs that received intravenous fluids and developed or did not develop fluid overload. Data are shown as frequency (%), along with the *p*-value for comparison of the two groups, odds ratio, and 95% confidence interval (95% CI).

	Fluid overload group ($n=136$)	Control group ($n=109$)	*p*	Odds ratio (95% CI)
Cardiovascular disease	46 (33.8%)	3 (2.8%)	<0.001	18.1 (5.4, 60.0)
Protein-losing nephropathy	17 (12.5%)	1 (0.09%)	<0.001	15.3 (2.0, 116.8)
Chronic kidney disease	30 (22.1%)	3 (2.8%)	<0.001	10.0 (3.0, 33.8)
Acute kidney injury	50 (36.8%)	11 (10.1%)	<0.001	5.2 (2.5, 10.6)
Metabolic disease	53 (39.8%)	13 (11.9%)	<0.001	4.9 (2.5, 9.6)
Gastrointestinal disease	85 (62.5%)	39 (35.8%)	<0.001	3.0 (1.8, 5.0)
Respiratory disease	33 (24.3%)	10 (9.2%)	0.002	3.2 (1.5, 6.8)
Sepsis	11 (8.0%)	4 (3.7%)	0.19	2.3 (0.7, 7.5)
Endocrine disease	11 (8.0%)	4 (3.7%)	0.19	2.3 (0.7, 7.5)
Neoplasia	19 (14.0%)	13 (11.9%)	0.64	1.2 (0.6, 2.6)
Surgery/orthopedic	8 (5.9%)	8 (7.3%)	0.65	0.8 (0.3, 2.2)
Neurologic disease	24 (17.6%)	27 (24.8%)	0.17	0.7 (0.4, 1.2)
Surgery/soft tissue	20 (14.7%)	37 (33.9%)	<0.001	0.3 (0.2, 0.6)
Trauma	3 (2.2%)	12 (11.0%)	0.004	0.2 (0.1, 0.7)

could have been missed. This definition also might have introduced bias into the classification of clinical signs of respiratory disease, especially because confirmatory diagnostic tests such as thoracic radiographs or echocardiography were not required for inclusion in the FO group.

In the human medical literature, FO commonly is defined as the "expansion of extracellular fluid volume with a positive fluid balance that produces a weight gain of greater than 10% from non-dehydrated baseline" [16–18]. However, this approach is prone to error because of the inaccuracy in charting weights and disagreement with whole body fluid balance [44, 45]. A study in dogs showed that dehydration assessment and predicted weight gain after fluid therapy are poorly correlated [46]. In our study, only 6.0% of dogs in the FO group met the FO definition used in human medicine of >10% increase from non-dehydrated baseline weight.

Conversely, 2.9% of dogs in the control group met this definition, despite having no clinical signs of FO. Those dogs could have developed subclinical FO and might have been misclassified. In our study, few dogs were managed using urinary catheters or drains, preventing calculation of the sum of cumulative fluid administration (ins) vs. the sum of cumulative losses via urine production, drainage losses, diarrhea, and insensible losses (outs), which are considered more accurate [30].

In addition to those previously mentioned, our study had limitations that are important to consider. Disease categories were assigned retrospectively to dogs based on clinical diagnoses described in the medical records without specific criteria for the diagnoses. Dogs also could be assigned to multiple disease categories. Therefore, the number of dogs in the various disease categories may be over- or under-estimated, and misclassification was possible. Because of the requirement to be hospitalized for a minimum of 3 days to meet inclusion criteria, certain disease categories might be underrepresented. Given the challenges of categorization of diseases and the relatively small number of patients in many of the categories, multivariable analysis was not possible, but would be valuable in future larger or prospective studies.

Because of the retrospective nature of our study, not all variables were available for every dog on every day of hospitalization (e.g., laboratory variables, body weight, variables required to calculate the APPLEfast score). This factor influenced the choice of statistical methods. Because the goal of our study was to generate hypotheses on potential mechanisms for FO in dogs rather than to test specific hypotheses, we opted against a multiple comparison correction. A type I error correction would have increased the chance of type II error and thus decreased the power of our study. Different statistical methods might have been able to better identify causality but carried the risk of losing the ability to identify differences between the groups. Future prospective studies may be able to better explore these associations.

In addition, the duration of hospitalization varied, and calculated changes in body weight included fewer dogs beyond Day 3. Data were not collected beyond the fifth day of hospitalization, and for dogs that were hospitalized longer than 5 days, it is unknown whether variables might have changed later during hospitalization. The control group (cases from January 1, 2020 to June 15, 2020) was from a different time frame than the FO group (2015–2020) because of the need to search a larger period to identify FO cases. Therefore, although the two groups were similar in age, sex, weight, and BCS, some differences in overall types of cases and treatments could have been present between the two groups. Furthermore, during the initial screening of records of dogs in 2020, only three cases with FO were identified over a 6-month period, whereas the second data query

identified more cases with clinical signs of FO. The increased number of cases with FO in the second half of 2020 (43/60 cases with FO admitted in 2020) as well as the difference in search criteria (development of FO based on clinician assessment in the medical record) could have introduced bias into case selection. Therefore, future studies should compare dogs with FO to controls from the same time period.

Subjective assessment of patients for variables such as percent dehydration, respiratory signs, and BCS was assessed and recorded by many different clinicians. Treatment plans including fluid therapy decisions were performed at the discretion of the attending clinicians and thus could have varied.

In conclusion, dogs with FO were more likely to have certain disease processes, such as cardiovascular disease, renal dysfunction, or metabolic, gastrointestinal, and respiratory disease. Dogs with FO were less likely to survive to discharge and had a longer median duration of hospitalization. However, FO was not associated with the volume of fluids administered IV. The definition of FO used in human medicine that relies on identification of a 10% weight gain needs to be further assessed in dogs to determine if it can be used as an indicator of FO in this species. Additional research focusing on the diagnosis of FO and development of safe fluid therapy protocols could help to decrease morbidity and mortality of hospitalized dogs receiving fluids IV.

Disclosure

Authors declare no off-label use of antimicrobials.

Ethics Statement

Authors declare no institutional animal care and use committee or other approval was needed. Authors declare human ethics approval was not needed.

Conflicts of Interest

The authors declare no conflicts of interest.

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