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Prevalence of and risk factors for intravenous catheter infection in hospitalized cattle, goats, and sheep

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Abstract

Background: Intravenous catheter (IVC) use in hospitalized ruminants is a common procedure. Limited information is available describing complications associated with IVCs.

Hypotheses: Prevalence of IVC infections in hospitalized ruminants is >50%. Intravenous catheters maintained for >5 days are more likely to be infected than those maintained for <5 days. Intravenous catheters placed non-aseptically have a higher risk for infection than those placed aseptically.

Animals: Thirty-four cattle, 39 goats, and 33 sheep were hospitalized in a university teaching hospital.

Methods: Prospective observational study. The IVCs from cattle, goats, and sheep admitted for medical and surgical procedures were randomly selected and submitted for bacteriological culture and susceptibility testing.

Results: Prevalence values (95% confidence interval) of infected catheters were 61.8 (45.5, 78.1), 51.3 (35.3, 66.7), and 42.4% (25.2, 58.8) in cattle, goats, and sheep, respectively. Coagulase-negative *Staphylococcus* spp was the most frequently isolated bacterium. Catheter type/placement technique was a significant (P = .03) predictor of IVC infection in goats but not in cattle (P = .65) and sheep (P = .47). Antibiotic use and reason for catheter placement were not significant predictors of IVC infection in all species. Catheters maintained for >4 days had a higher likelihood of being infected than those maintained for <4 days in all species.

Conclusions and Clinical importance: Clinicians should consider replacing catheters maintained for >4 days to reduce IVC infection.

KEYWORDS
antibiotic, aseptic, bacteria, coagulase-negative *Staphylococci*

1 | INTRODUCTION

Use of IV catheters (IVCs) in hospitalized cattle, goats, and sheep is a common medical procedure for administering fluids, parenteral nutrition, and drugs. In human patients, IVC placement is associated with

blood stream infections leading to increased prevalence of nosocomial infections resulting in increased hospitalization costs, high morbidity, and mortality rates.[1] Risk factors for IVC infections in human patients include underlying disease, site of catheter placement, duration of placement, purpose of catheterization, and poor personal hygiene.[1,2] In human patients, complications associated with IVC infections include phlebitis,[3] bacteremia, and septicemia.[1]

Reported incidence of IVC infection in dogs and cats range from 15.4 to 22%.[4-6] In dogs, bacteria isolated from IVCs are of gastrointestinal or environmental origin[4] with *Staphylococcus* spp[5] and *Acinetobacter* spp[6] being the most frequently isolated bacteria. Furthermore, the bacteria isolated from IVCs in dogs are multidrug resistant,[4] suggesting a negative impact on antibiotic treatment outcomes. When compared to humans and dogs, cattle, goats, and sheep are exposed to similar risk factors for complications after IVC placement; however, difficulty in maintaining optimal hygiene in hospital stalls may play a larger role in ruminant species. Complications after IVC placement in cattle include *Staphylococcus* spp infection of the catheter[7] and thrombophlebitis.[7-9] In an experimental model in pregnant sheep, long-term IVC placement is a risk factor for abortion after infection of the catheters by *Staphylococcus aureus*.[10]

Limited literature is available describing the risk factors for IVC infections, and identification of bacteria associated with IVC infections in hospitalized goats and sheep. Furthermore, limited literature is available describing susceptibility patterns of bacteria isolated from IVCs in hospitalized cattle. We hypothesized that (1) the prevalence of IVC infections in hospitalized cattle, goats, and sheep is >50%; (2) IVCs maintained for >5 days are more likely to be infected compared to those maintained for <5 days in cattle, goats, and sheep; and (3) IVCs placed in a non-aseptic (using non-sterile gloves) manner have a higher likelihood for infection compared to those placed in an aseptic manner (using sterile gloves). The objectives of this study were to determine the prevalence of IVC infections, identify risk factors associated with IVC infections, identify the bacteria associated with IVC infections, and their susceptibility patterns, in hospitalized cattle, goats, and sheep.

2 | MATERIALS AND METHODS

2.1 | Animals and experimental design

A prospective, observational, nonrandomized study was conducted. The sample size was calculated based on a hypothesized prevalence of 10% of peripheral IVC infections in cattle, goats, and sheep, compared to studies in dogs that reported a prevalence of approximately 22%,[4] alpha = .05, and a power of 80%. A statistical software (JMP, SAS Institute, Cary, North Carolina) was used to estimate the sample size. The minimum sample size required for each species was 27 animals. To account for a 20% (~6 animals) dropout because of lost or contaminated IVC samples, 6 additional animals were added to each species. The final sample sizes required were 33 cattle, 33 goats, and 33 sheep.

Cattle, goats, and sheep admitted to the Veterinary Medical Teaching Hospital (VMTH) and hospitalized for various medical and surgical conditions that required placement of a peripheral IVC for at least 24 hours were enrolled. Signalment of the patient including age, breed, and use was recorded. The clinical diagnosis, and the reason for placement of the IVC indicated as medical, or surgical, or both was recorded. The study was conducted between May 2017 and June 2018. The study was approved by the Institutional Animal Care and Use Committee (#19736).

2.2 | Sample collection

2.2.1 | Catheter placement and care

Catheter placement preparation procedures were similar in all cases. The external jugular vein catheter site in the left or right side was clipped and prepared aseptically. The site was scrubbed with a povidone-iodine (BD E-X Scrub 205, Becton Dickinson and Company, Franklin Lakes, New Jersey) scrub brush for 5 minutes. The site was then wiped with alternating povidone iodine (10%, Vet One, Boise, Idaho) solution, and alcohol-soaked gauze (70% isopropyl rubbing alcohol, Humco, Texarkana, Texas), 3 times. The insertion site for the IVC was then anesthetized with 10-20 mg of 2% lidocaine (2% lidocaine, Vet One) for all patients followed by a final preparation with 2 alternating povidone-iodine solution and alcohol-soaked gauzes. A 3-5 mm skin incision was performed before insertion of both catheter types to aid placement. Sterile gloves were worn for placement of over-the-wire type catheters (Arrow catheter, Arrow International Inc, Reading, Pennsylvania) whereas non-sterile examination gloves were worn for second catheter type (Mila catheter extended use, Mila International Inc, Florence, Kentucky). The IVC type and size used depended on the clinical diagnosis and patient size. Arrow catheters used included 14-gauge × 8-inch (n = 22), and 16-gauge × 8-inch (n = 56) sizes. Mila catheters used included 12-gauge × 5.25-inch (n = 2), 14-gauge × 5.25-inch (n = 1), and 16-gauge × 3.25-inch sizes (n = 25). Goats and sheep had either a 14-gauge × 8-inch, 16-gauge × 8-inch arrow catheter or a 16-gauge × 3.25-inch Mila catheter placed. Cattle had any 1 of the previously described catheters placed. Choice of catheter was based on clinician preference. Clinicians' bias toward use of the Arrow type catheter was based on anecdotal experience that the Arrow type catheter maintained patency longer, and was more cost effective. Catheter care included flushing of the catheter with heparinized saline every 4-6 hours if not used for continual fluid administration. Clean examination gloves were worn by personnel, and a new syringe of heparinized saline drawn from a communal 250 mL bag with a new needle was used each time for flushing. If not finished after 24 hours of use, the heparinized saline bags were discarded, and a new bag was prepared. A variety of personnel flushed the catheters including veterinary students, technicians, and clinicians. Injection caps were not regularly changed or cleaned unless deemed necessary. If the IVC was used for continual fluid administration, monitoring was performed using a fluid pump to ensure patency of the IVC. The majority of patients in the study received a

combination of continuous fluid administration and catheter flushing with heparinized saline every 4-6 hours. On presentation, and during daily physical examination of the animals while catheterized cattle with a rectal temperature >39.2°C (>102.5°F) were considered febrile, whereas sheep and goats with a rectal temperature >39.7°C (>103.5°F) were considered febrile.

2.2.2 | Catheter removal

When the catheter was no longer required or was no longer patent, it was removed without contacting the animal, and the distal 5 cm of the catheter was cut with sterile scissors and placed in a sterile transport cup. Cleaning preparation was not performed on the site before catheter removal. The catheter was then submitted to the VMTH Microbiology Laboratory for bacteriological culture and susceptibility testing.

2.3 | Catheter sample analysis

Aerobic culture and susceptibility testing were performed according to the Clinical and Laboratory Standard Institute guidelines.[11] Catheter samples with >15 colony forming units of bacteria were considered infected.[3] Catheters were gently rolled on to the surface of 1 quadrant of 5% sheep blood agar (Hardy Diagnostics, Santa Maria, California) and then the agar was streaked for isolation. In order to isolate fastidious organisms, a "feeder" streak of *S. aureus* was applied from the first to third quadrants of the agar surface. Plates were incubated inverted at 35°C in 5% CO_2 and examined daily, for growth. Plates were incubated for a total of 5 days before determination of no growth. Isolated bacteria were identified by use of a variety of methods including colony appearance, hemolytic pattern, Gram staining characteristics, spot testing (catalase, oxidase, indole), matrix-assisted laser-desorption-ionization time of flight mass spectrometry (Bruker Daltonics, Billerica, Massachusetts), API identification strips (bioMereiux, Durham, North Carolina), and tubed media for conventional biochemical analyses.

Antimicrobial susceptibility testing was performed using the broth microdilution technique using Sensititre susceptibility equipment (ThermoFisher Scientific, Waltham, Massachusetts). Briefly, 2-4 colonies of isolated bacteria were inoculated into 2 mL of brain heart infusion broth (Biological Media Service, University of California, Davis, California) and incubated at 35°C under ambient atmosphere for 3-5 hours. Broth cultures were added dropwise to 0.85% saline to reach a McFarland standard of 0.5 as determined by a nephelometer (Sensititre, ThermoFisher Scientific). Ten microliter of the inoculated saline was then transferred to a cation-adjusted Mueller-Hinton broth or cation-adjusted Mueller-Hinton broth with lysed horse blood (Sensititre, ThermoFisher Scientific) for fastidious organisms such as *Pasteurellaceae* or *Streptococci*. Fifty microliter of Mueller-Hinton broth was inoculated into each well of a standard food animal antimicrobial susceptibility panel. Panels

were sealed and incubated at 35°C without CO_2 for 18 hours (24 hours for oxacillin resistance) before reading to determine the minimum inhibitory concentration for each drug.

2.4 | Statistical analysis

Descriptive statistics including prevalence of IVC infection, identity of the bacteria and susceptibility patterns were determined. Association between catheter type/placement technique (non-aseptic Mila or aseptic-Arrow), reason for placing the catheter (medical, surgical, or medical and surgical), and use of antibiotics (yes or no), with IVC catheter infection (yes or no) was evaluated using the χ^2 test or Fisher's exact test when a cell in the 2×2 frequency table had counts <5. Association between the presence of fever recorded on presentation or at least once while animals were catheterized, and IVC infection in all species was evaluated with a χ^2 test. In cases where a cell had zero counts, 0.5 was added to all cells.

For each species, a follow-up forward stepwise multivariate logistic regression model predicting the probability of an IVC infection (yes or no) as a function of the following explanatory variables; type of catheter used (non-aseptic-Mila or aseptic-Arrow), reason for placing catheter (medical, surgical, or medical and surgical), use of antibiotics (yes or no), and duration of catheter placement (1-2, >2-4, or >4 days) was performed. Determination of intervals for duration for catheter placement were based on initial data diagnostics using scatter plots and determination of the distribution of duration (days) of IVC placement. All explanatory variables were first explored with univariate analysis based on their presumed association with IVC infection. Unanticipated confounders of the outcome of interest (IVC infection) were investigated, reported, and or controlled, when possible. In the logistic regression, dummy variables were created to code the levels of the categorical explanatory variables. First-order interactions between the explanatory variables were considered when appropriate. Initial entry into the logistic regression model was set $P = .1$ but final model significance was set at $P = .05$. The significance of the final model was assessed using maximum likelihood estimation. The general logistic regression model was summarized by the following equation:

$$\text{Probability of an IVC infection} = 1 \Big/ \left[1 + e^{-(b_0 + b_1 X_1 + b_n X_n)} \right]$$

where e is the exponential function; b_0 denotes constant for the model; b_1 and b_n are the coefficients for the explanatory variables; and X_1 and X_n are explanatory variables.

A statistical software (JMP Pro version 14.2, SAS Institute) was used to analyze the data. In all analyses $P < .05$ was considered significant.

Positive interval likelihood ratios (LHR+) and 95% confidence interval (95% CI)[12,13] were calculated to determine the duration of IVC placement that increased the likelihood of infection using the following formula:

$$\text{LHR} + = \frac{\text{Probability of IVC infection given the duration of placement}}{\text{Probability of no IVC infection given the duration of placement}}$$

Interval likelihood ratios >1 with a 95% CI excluding 1 indicated an IVC placement duration that increased the likelihood of infection of the IVC. Likelihood ratios <1 with a 95% CI excluding 1 indicated an IVC placement duration that decreased the likelihood of infection of the IVC. Likelihood ratios = 1, indicated no effect of the IVC placement duration and infection of the IVC.

3 | RESULTS

3.1 | Prevalence of IVC infection and susceptibility patterns

Samples from 34 cattle, 39 goats, and 33 sheep were available for analysis. Median (range) of age in the sample population for all species was 2 years (2 hours to 18 years). Proportion of IVCs placed for medical reasons alone were 85% (29/34), 54% (21/39), and 49% (16/33) in cattle, goats, and sheep, respectively. Proportion of IVCs placed for surgical reasons alone were 15% (5/34), 15% (6/39), and 30% (10/33) in cattle, goats, and sheep, respectively. Proportion of IVCs placed for a combination of medical and surgical reasons were 0% (0/34), 31% (12/39), and 21% (7/33) in cattle, goats, and sheep, respectively. Prevalence of infected IVCs were 62% (21/34; 95% CI: 45.5, 78.1), 51% (20/39; 95% CI: 35.3, 66.7), and 42% (14/33; 95% CI: 25.2, 58.8) in cattle, goats, and sheep, respectively.

Of the 53 culture-positive catheters where records of temperature were obtained for all species, 31 of those patients were febrile at least once at presentation, during hospitalization, or both presentation and during hospitalization. Twenty-two were afebrile during this period. Of the 43 culture negative catheters where records of temperature were obtained for all species, 22 were febrile at least once at presentation, during hospitalization, or both presentation and during hospitalization. Twenty-one were afebrile during this period. There was no association between presence of fever and proportion of infected IVCs (P = .54).

The identity of pathogens isolated from the IVC in cattle, goats, and sheep are summarized in Table 1. Proportion of IVCs with more than 1 bacterium genus isolated were 18% (6/34), 3% (1/39), and 6% (2/33) in cattle, goats, and sheep, respectively. Coagulase-negative *Staphylococcus* spp (CNS) was the most frequently isolated bacteria from the IVCs in cattle, goats, and sheep (Table 1). Because of the low frequency of other bacteria, only CNS susceptibility patterns are reported. Susceptibility patterns were considered for antibiotics commonly used in food producing animals including ampicillin, ceftiofur, penicillin, and tetracycline. Susceptibility patterns to macrolides, fluoroquinolones, and florfenicol were not reported because of lack of specific break points for CNS. In cattle, 71%, 100%, 100%, and 43% of the CNS isolates were resistant to ampicillin, ceftiofur, penicillin, and tetracycline, respectively. In goats, 90%, 100%, 100%, and 30% of CNS isolates were resistant to ampicillin, ceftiofur, penicillin, and tetracycline, respectively. In sheep, 83%, 100%, 100%, and 83% of CNS isolates were resistant to ampicillin, ceftiofur, penicillin, and

TABLE 1 Summary of frequency and identification of bacteria isolated from infected intravenous catheters in hospitalized cattle (N = 34), goats (N = 39), and sheep (N = 33)

Pathogen	Cattle	Goats	Sheep
Aerococcus viridans	1	1	0
Citrobacter freundii	1	0	0
Coagulase-negative *Staphylococcus* group	9	10	6
Coagulase-positive *Staphylococcus* group	2	0	0
Escherichia coli (non-hemolytic)	2	0	1
Enterobacter cloacae	0	2	0
Enterococcus faecalis	1	0	0
Gram-positive bacilli	1	2	0
Gram-positive rod catalase +	0	0	1
Klebsiella pneumoniae	1	0	0
Moraxella spp	1	0	0
Non-enterobacteriaceae	1	0	1
Pantoea species	0	0	1
Pasteurella spp	0	1	0
Proteus mirabilis	2	0	0
Pseudomonas aeruginosa	0	0	1
Salmonella dublin	1	0	0
Staphylococcus aureus	0	1	3
Staphylococcus intermedius	1	0	0
Staphylococcus hyicus	1	0	0
Staphylococcus pseudointermedius	0	0	1
Staphylococcus spp	0	0	1
Stenotrophomonas maltophilia	0	1	0
Streptococcus viridans group	1	0	0
Streptococcus suis	1	0	0
Streptococcus uberis	1	0	0
Trueperella pyogenes	1	0	0

tetracycline, respectively. Frequency of infected catheters relative to body systems affected in cattle, goats, and sheep are summarized in Table 2. The highest percentages of culture-positive catheters were recorded in those admitted for gastrointestinal (83.33%), urinary (100%), and musculoskeletal (60%) reasons in cattle, goats, and sheep, respectively.

3.2 | Association among reasons for placing IVC, catheter type, use of antibiotics, and IVC infection

Reasons for placing IVCs and associated body systems affected by the disease conditions in cattle, goats, and sheep are summarized in Table 2. There was no association between the reason for placing the catheter (medical versus surgical versus medical and surgical) in cattle (P = .94), goats (P = .88), or sheep (P = .41), and the proportion of infected IVCs. Proportion of cattle, goats, and sheep catheterized with Mila type were 12% (4/34), 33% (13/39), and 67% (22/33), respectively. Proportion of cattle, goats, and sheep catheterized with Arrow type were 88%

TABLE 2 Summary of the frequency of infected intravenous catheters, associated body systems affected, and reasons for placement for catheter placement in cattle (N = 34), goats (N = 39), and sheep (N = 33)

	Cattle		Goats			Sheep		
	Medical	Surgical	Medical	Surgical	Medical and surgical	Medical	Surgical	Medical and Surgical
Urinary	0/0	0/0	5/5	0/0	3/8	0/0	0/0	0/1
Respiratory	2/6	0/0	2/2	0/0	0/0	1/2	0/0	0/0
Gastrointestinal	10/12	0/0	1/7	1/1	0/1	0/0	0/0	0/0
Neurological	0/0	0/0	2/4	0/0	0/0	0/0	0/0	0/0
Reproductive	2/2	2/2	0/0	0/1	0/1	0/1	5/10	1/1
Mammary	0/0	0/0	0/0	0/2	0/0	0/1	0/0	0/0
Musculoskeletal	0/3	2/3	0/0	1/1	1/2	1/1	0/0	2/4
Metabolic	2/5	0/0	0/0	0/0	0/0	0/1	0/0	0/0
Hepatic	0/0	0/0	0/0	0/0	0/0	0/1	0/0	0/0
Neoplastic	0/0	0/0	1/1	0/0	0/0	0/0	0/0	0/0
Systemic infection	0/0	0/0	0/0	0/0	0/0	3/7	0/0	0/0
Anorexia	0/1	0/0	1/1	0/0	0/0	0/2	0/0	0/0
Ophthalmic	0/0	0/0	0/0	1/1	0/0	0/0	0/0	0/0

Notes: The first digit in each cell represents the number of infected catheters, whereas the second digit represents the total number of catheters submitted from animals with the affected body system, for each species. For instance, 10 of 12 catheters from cattle diagnosed with medical gastrointestinal disorders were infected.

Variable	Coefficient	SE	Odds ratio (95% CI)	P
Intercept	−0.53	0.44		
Aseptic-Arrow	Referent			
Non-septic Mila	2.22	0.92	9.27 (1.52, 56.5)	.02
1-2 days Catheter duration	Referent			
Catheter duration	−1.12	0.61	0.32 (0.11, 0.98)	.03

TABLE 3 Final model predicting the probability of infection of an intravenous catheter in goats (N = 39)

Note: Two levels (2 dummy variables) were created for the catheter type/procedure (aseptic-Arrow or non-septic Mila) and 3 levels (3 dummy variables) were created for the catheter duration (1-2, >2-4, or >4 days).
Abbreviation: 95% CI, 95% confidence interval.

(30/34), 67% (26/39), and 33% (11/33), respectively. There was no association between the catheter type/placement technique in cattle (*P* > .99), goats (*P* = .18), or sheep (*P* = .28) and proportion of infected IVCs based on the χ^2 test. Proportions of animals administered antibiotics were 82% (28/34), 97% (38/39), and 97% (32/33), for cattle, goats, and sheep, respectively. There was no association between administration of antibiotics in cattle (*P* = .63), goats (*P* > .99) or sheep (*P* > .99) and proportion of infected IVCs.

The final logistic regression model for goats had a significant fit (*P* = .03). Duration of IVC placement (*P* = .04) and catheter/placement technique (*P* = .02) were significant predictors of IVC infection in goats. Reasons for IVC placement (*P* = .48) and treatment with antibiotics (*P* = .99) were not significant predictors of infection in goats.

Probability of an IVC infection in goats was

$$= 1 / \left[1 + e^{-(-0.53 + 2.2 \times \text{Mila/non-aseptic} - 1.12 \times \text{Catheter duration})} \right]$$

In goats, the probability of IVC infection increased when Mila/non-aseptic catheters were placed and maintained for longer time

periods compared to when Arrow-aseptic catheters were used (0.84 versus 0.37 for 1-2 days, 0.63 versus 0.16 for >2-4 days, and 0.94 versus 0.64 for >4 days). None of the possible first-order interactions among the explanatory variables were significant.

The final logistic regression equation for goats is summarized in Table 3. The final logistic regression models for cattle (*P* = .65) and sheep (*P* = .47) were not significant.

3.3 | Duration of catheter placement

Median (range) for duration of maintenance of IVCs was 2.8 (1-21), 4 (1-9), and 3 (1-7) days for cattle, goats, and sheep, respectively. The likelihood for infection of IVCs maintained for >4 days were 3.7 (LHR = 3.7; 95% CI, 2.4-5.8), 2.2 (LHR = 2.2; 95% CI, 1.3-3.8), and 5.4 (LHR = 5.4; 95% CI, 3.0-10.4) times more likely than the likelihood of no infection in cattle, goats, and sheep, respectively. In goats, the likelihood for infection of IVCs maintained for 2-4 days was 0.5 (LHR = 0.5; 95% CI, 0.3-0.9) times more likely than the likelihood of

TABLE 4 Summary of positive interval likelihood ratios predicting infection of intravenous catheters maintained for different time periods in hospitalized cattle (N = 34)

Time to catheter removal	Number of catheters in the strata	Infected catheters	Non-infected catheters	Likelihood ratio (95% CI)
1-2 days	16	9	7	0.80 (0.49-1.30)
>2-4 days	11	6	5	0.74 (0.43-1.31)
>4 days	7	6	1	3.71 (2.38-5.78)
Total	34	21	13	

Notes: Likelihood ratio for catheters placed for 1-2 days: 9/21÷7/13 = 0.8. Likelihood ratio for catheters placed for >2-4 days: 6/21÷5/13 = 0.74. Likelihood ratio for catheters placed for >4 days: 6/21÷1/13 = 3.71. Interval likelihood ratios >1 with a 95% CI excluding 1 indicated an IVC placement duration that increased the likelihood of infection of the IVC. Likelihood ratios <1 with a 95% CI excluding 1 indicated an IVC placement duration that decreased the likelihood of infection of the IVC. Likelihood ratios = 1, indicated no effect of the IVC placement duration and infection of the IVC. Abbreviations: 95% CI, 95% confidence interval; IVC, intravenous catheter.

TABLE 5 Summary of positive interval likelihood ratios predicting infection of intravenous catheters maintained for different time periods in hospitalized goats (N = 39)

Time to catheter removal	Number of catheters in the strata	Infected catheters	Non-infected catheters	Likelihood ratio (95% CI)
1-2 days	15	8	7	1.09 (0.66-1.78)
>2-4 days	14	5	9	0.53 (0.32-0.88)
>4 days	10	7	3	2.22 (1.29-3.81)
Total	39	20	19	

Notes: Likelihood ratio for catheters placed for 1-2 days: 8/20÷7/19 = 1.09. Likelihood ratio for catheters placed for >2-4 days: 5/20÷9/19 = 0.53. Likelihood ratio for catheters placed for >4 days: 7/20÷3/19 = 2.22. Interval likelihood ratios >1 with a 95% CI excluding 1 indicated an IVC placement duration that increased the likelihood of infection of the IVC. Likelihood ratios <1 with a 95% CI excluding 1 indicated an IVC placement duration that decreased the likelihood of infection of the IVC. Likelihood ratios = 1, indicated no effect of the IVC placement duration and infection of the IVC. Abbreviations: 95% CI, 95% confidence interval; IVC, intravenous catheter.

TABLE 6 Summary of positive interval likelihood ratios predicting infection of intravenous catheters maintained for different time periods in hospitalized sheep (N = 33)

Time to catheter removal	Number of catheters in the strata	Infected catheters	Non-infected catheters	Likelihood ratio (95% CI)
1-2 days	16	5	11	0.62 (0.37-1.03)
>2-4 days	12	5	7	0.97 (0.56-1.68)
>4 days	5	4	1	5.43 (2.95-10.43)
Total	33	14	19	

Notes: Likelihood ratio for catheters placed for 1-2 days: 5/14÷11/19 = 0.62. Likelihood ratio for catheters placed for >2-4 days: 5/14÷7/19 = 0.97. Likelihood ratio for catheters placed for >4 days: 4/14÷1/19 = 5.43. Interval likelihood ratios >1 with a 95% CI excluding 1 indicated an IVC placement duration that increased the likelihood of infection of the IVC. Likelihood ratios <1 with a 95% CI excluding 1 indicated an IVC placement duration that decreased the likelihood of infection of the IVC. Likelihood ratios = 1, indicated no effect of the IVC placement duration and infection of the IVC. Abbreviations: 95% CI, 95% confidence interval; IVC, intravenous catheter.

no infection. Calculated interval likelihood ratios for IVC infection in cattle, goats, and sheep are summarized in Tables 4–6, respectively.

4 | DISCUSSION

The prevalence of IVC infection in our study was high in cattle and goats, consistent with our hypothesized prevalence of >50%. Although <50%, the prevalence of IVC infection in sheep was still relatively high (42%). Our study focused on estimating prevalence of IVC infection whereas previous studies in cattle focused on determining the presence of thrombophlebitis as a risk for IVC infection.[7-9] Although

thrombophlebitis is a risk for IVC infection, interpretation of our study results and previous studies in cattle might not be directly comparable. The prevalence in the previous study in sheep[10] was higher (61.9%) than in our study possibly because of the longer duration (>24 days) of catheter maintenance. Comparable studies determining prevalence of IVC infections are not available in goats. We chose to focus our study on IVC infections because of potential bacteremia and septicemia secondary to IVC infection. We anticipate that the risk for spread of bacteria and bacterial toxins from the infected catheter will be enhanced by the flow of fluids administered IV or heparinized saline being administered to the cattle, goats, and sheep as demonstrated in the experimental sheep model.[10]

In our study, non-aseptically placed Mila catheters were associated with increased IVC infection in goats consistent with our hypothesis, and consistent with studies in human patients.[14] In contrast, catheter type/placement technique was not associated with increased IVC infection in cattle and sheep. Our study results in cattle and sheep are consistent with studies in dogs and cats,[15] but in contrast to studies in human patients, which reported that specific catheter types were associated with increased risk of bacterial infections.[14] A possible explanation for the lack of significance of the catheter type/placement technique as a risk factor for IVC infection in cattle and sheep might be that adequate skin preparation, as in our study, before catheter placement significantly reduces risk of IVC infection. In cattle, the reported risk for IVC infection was significantly reduced when skin preparation of the IVC site was performed similar to when an animal is prepared for surgery.[7] In contrast, inadequate skin preparation was a cause of IVC-related infections in dogs.[16]

In vitro studies demonstrated that catheters made of polyvinyl chloride or polyethylene are likely less resistant to adherence by microorganisms compared to catheters made of Teflon, silicon elastomer, or polyurethane.[17,18] The Arrow and Mila type catheters used in this study are both made of polyurethane. This material is likely resistant to bacterial adherence and this might have contributed to lack of catheter type/placement technique effect in cattle and sheep. Furthermore, some IVC materials have surface irregularities that enhance microbial adherence of bacteria such as CNS and *Pseudomonas aeruginosa*.[19-21] Consequently, the lack of difference in proportions of infected IVCs between the 2 catheter types/placement technique used in cattle and sheep could also have been as a result of similar surface irregularities in the materials used to make the catheters. Polyethylene catheters were not used in our study as they are not routinely stocked in our hospital; hence, we are not able to make similar comparisons. It is important to note that the prevalence of IVC infection was high in all species despite catheters being made of polyurethane suggesting that the risks for IVC infection are multifactorial.

We did not determine the association between specific medical or surgical procedures or the infusate type administered, and IVC infection because of the relatively low number of animals recorded for each specific procedure or infusate. Furthermore, in some cases, a single animal was administered with more than 1 classification of infusate, for instance, colloids such as whole blood, followed by crystalloids. In dogs, the infusate type including total parenteral nutrition, partial parenteral nutrition, dextrose, blood products, and fluids for oncotic support was not associated with IVC infection.[15] In contrast, an increase in IVC infections was reported when fluids that enhance microbial growth such as lipid emulsions and blood products were administered in human patients.[22,23]

Our results differ from human patient studies that reported a protective effect against IVC infections when systemic antibiotics were administered.[2] Although studies in human patients reported protective effects against IVC infections when a heparin-antibiotic combination flushing of the IVC was used,[24,25] such antibiotics (vancomycin) are prohibited for use in food producing animals. In our study

population, a significant (>80%) proportion of the animals administered antibiotics. Thus, the lack of association between administration of antibiotics and IVC infections might be as a result of low number of patients not administered antibiotics.

Catheters maintained for >4 days had a higher likelihood of infection than those maintained for ≤4 days, consistent with our hypothesis. Our results are consistent with studies in human patients, which reported an increase risk of bacterial colonization when IVCs were left in place for >3 days[3,26-28] and 4 days.[29] In contrast, the duration of IVC maintenance was not a significant risk factor for IVC infection in dogs and cats managed in an intensive care unit.[15] Coagulase-negative *Staphylococci*, a common skin inhabitant, was most frequently isolated from IVCs, consistent with studies in human patients.[3,30-32] In cattle, *Staphylococcus chromogenes* and *Staphylococcus xylosus*[7] were the most frequently isolated pathogens, whereas *S. aureus*[10] was the most frequently isolated pathogen in sheep IVCs. In catheters maintained for a short period, the most common route of infection of IVCs is by migration of skin inhabitants at the IVC insertion site into the catheter tract followed by colonization of the catheter tip.[30,33] In catheters maintained for longer periods, contamination of the IVC hub contributes to intraluminal colonization,[34-36] but occasionally IVCs can be infected hematogenously from another infection site.[37] Coagulase-negative *Staphylococcus* can adhere to polymer surfaces such as an IVC more readily[37] secrete an extracellular polysaccharide,[38,39] and can form a biofilm which protects the bacteria from the effects of antimicrobials and the host immune system.[40,41] A high proportion of the CNS isolates in our study were resistant to multiple antibiotics commonly used in food producing animals, suggesting that CNS should be considered a potential nosocomial infection in animals with IVCs. In our study, *Salmonella dublin* was isolated from a single bovine IVC, however *S. dublin* was also isolated from the blood culture of this animal, and the animal was admitted after an outbreak of *S. dublin* on the farm of origin. Thus, the IVC infection in this animal was not considered a nosocomial infection.

The practical clinical implications of the results of our study include informing clinicians of the high prevalence of IVC infections in hospitalized ruminants, resistance of CNS to multiple antibiotics labeled for use in food producing animals, and consideration to replace catheters maintained for >4 days to reduce IVC infection. In goats, aseptic catheter site preparation should be considered to reduce IVC infections. A potential reason why catheter type/placement technique was a significant predictor of IVC infection in goats compared to cattle or sheep is their relatively curious contact behavior with examiners or inanimate objects in the hospital environment along with an increased tendency to chew their fluid administration sets, thereby increasing the likelihood of infection of the IVC. In the event that a goat chews the administration set, clotting might occur in the absence of continuous fluid administration. None of the goats in our study were re-catheterized because of lack of IVC patency. It is important to note that the association between catheter type/placement techniques for goats was not significant based on the χ^2 test but significant based on the logistic regression. This is because χ^2 test can only evaluate a relationship between variables, whereas the logistic regression can evaluate relationship

between variables, allows concurrent evaluation of several continuous and categorical variables, evaluates interactions between variables, and predict an outcome.[42]

Our study has limitations, including the presence of potential confounders. We did not record the physical examination findings for evidence of significant inflammation or perform ultrasonography, at the catheter site, upon catheter removal. As a result, an association between bacteriological culture of the IVC and results of physical or ultrasonographic examination findings was not determined. We did not analyze the IVC site examination findings because of the inconsistencies in classifying whether the site findings were significant or not. There is no standardized scale for determining significant IVC site catheter findings based on physical examination. Although thrombophlebitis is a risk for IVC infection, our focus was on other risk factors for IVC infections. Similarly, we did not account for the catheter placer as a variable. In our study, catheters were placed by different clinicians, residents, and students with varying levels of experience. Studies in human patients reported an increased risk for IVC infections when placed by a clinician who had previously placed <50 catheters.[43] In cattle, the placement of a catheter by a less experienced individual increased the risk for development of thrombophlebitis.[9] Thrombophlebitis can serve as a nidus for bacterial growth and subsequent IVC infection. Therefore, the variety of catheter placers, with variable experiences, may have increased the catheter infection rate in our study as more experienced personnel are likely to adhere to aseptic technique and cause less trauma upon IVC insertion because of a fewer number of attempts. Our study was performed in a teaching hospital setting, where catheter placement is a required clinical competency expected of students on the livestock medicine and surgery clinical rotation. Therefore, controlling for experience of the IVC placer was not possible in our study. Controlling for the catheter placer should be considered in future studies. Furthermore, our study did not assess the association between risk of IVC infection and severity of disease diagnosed on initial examination because of lack of a reliable severity scoring system for multiple organ systems. Studies in humans demonstrated an increased catheter-associated attributable mortality in patients with severe disease on presentation, compared to controls.[44]

Presence of an IVC infection does not equate development of bacteremia. We did not perform blood cultures and therefore we were not able to assess the association between IVC infection and evidence of bacteremia. Future studies should consider investigating the association between bacteriological culture from IVCs and blood culture results. Concurrently, catheter sites could be examined by palpation or ultrasonography for evidence of thrombophlebitis. The association between the presence of thrombophlebitis and bacterial culture results from the IVCs also should be investigated.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

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

The study was approved by the University of California Davis Animal Care and Use Committee (#19736).

HUMAN ETHICS APPROVAL DECLARATION

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

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