Association between hoof lesions and fertility in lactating Jersey cows

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ABSTRACT

The objectives of this study were to evaluate the association between hoof lesions and fertility in dairy cows. Lactating Jersey cows ($n = 1,639$) were enrolled at 20 ± 3 d in milk (D20), examined and treated for presence of hoof lesions (HL), and evaluated for body condition score (BCS). Afterward, they were managed according to standard farm procedures, including estrus detection and presynchronization and a 5 d Co-synch-72 protocol for cows that failed to show estrus. Ovaries were scanned at 27 and 41 ± 3 d in milk, and cows with a corpus luteum greater than 20 mm on at least 1 exam were considered cyclic. At 120 ± 3 d in milk (D120), cows were re-examined for HL and BCS. Cows were classified at D20 according to HL status as healthy ($n = 1,197$) or having HL ($n = 429$), and according to HL category as healthy ($n = 1,197$) or having a sole hemorrhage ($n = 280$), noninfectious HL (sole ulcer, toe ulcer, or white line disease; $n = 113$), or infectious HL (digital dermatitis and foot rot; $n = 36$). Cows with HL at D20 had reduced odds of being cyclic (38.3 vs. 51.9%) and a longer interval from calving to first service (58 vs. 51 d) compared with healthy cows. Cows with infectious HL at D20 had reduced odds of pregnancy to first service (16.7 vs. 38.3%) compared with healthy cows. Cows with sole hemorrhage at D20 were more likely to lose pregnancies between d 32 and 64 after the first service postpartum compared with healthy cows (10.5 vs. 5.2%). Cows with sole hemorrhage at D20 had a smaller hazard of pregnancy (67.9 vs. 75.5%) at 150 d in milk and more days open (88 vs. 77d) compared with healthy cows. To assess the relationship between the development of HL and fertility, cows were classified as healthy (no HL at D20 and D120; $n = 308$), cured (any HL at D20 and no HL at D120; $n = 72$), new HL (no HL at D20 and any HL

at D120; $n = 597$), and chronic (any HL at D20 and D120; $n = 226$). Sole hemorrhage accounted for 93% of new HL. The proportions of cows with HL at D20 and D120 were 26.9 and 68.4%, respectively. We found no evidence for a difference in pregnancy hazard at 150 d in milk between cows that remained healthy ($n = 308$) and cows that developed new HL ($n = 597$). Hoof lesions at D20, but not new HL, were associated with decreased odds of cyclicity, longer interval from calving to first service postpartum, and reduced pregnancy hazard in Jersey cows. The effect of an HL diagnosis in early lactation and management to reduce chronic HL in dairy cows warrants further investigation.

Key words: lameness, hoof lesion, foot trim, cyclicity, pregnancy hazard

INTRODUCTION

Lameness is an important disease that affects the welfare of dairy cows worldwide (Huxley, 2013). It is a debilitating health condition associated with significant economic losses (Cha et al., 2010) and behavioral changes (Alsaad et al., 2017; Weigle et al., 2018). The average cost per case of lameness ranges between \$120 and \$216; lameness caused by sole ulcers is more costly than infectious lesions such as digital dermatitis and foot rot (interdigital phlegmon; Cha et al., 2010). Hoof lesions are responsible for over 90% of lameness (Murray et al., 1996; Phillips, 2002) and can be categorized as noninfectious lesions (such as sole hemorrhage, sole ulcer, or white line disease) or infectious lesions (digital dermatitis and foot rot; Cramer et al., 2008). In North America, the prevalence of hoof lesions (HL) ranges from 20 to 37% and varies considerably among housing systems and farms (Cramer et al., 2009; Solano et al., 2016).

Studies of the relationship between lameness and reproductive performance show conflicting effects (Garbarino et al., 2004; Morris et al., 2011; Aungier et al., 2014) and focus on lameness defined by locomotion scoring, not HL. Visual locomotion score is subjective (Schlager-Tello et al., 2014) and may lack concor-

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dance with visible HL (García-Muñoz et al., 2016). Several studies have evaluated the resumption of ovarian activity (Garbarino et al., 2004; Aungier et al., 2014), interval from calving to first service interval (Melendez et al., 2003; Machado et al., 2010; Morris et al., 2011), and conception to first service (Barkema et al., 1994; Bicalho et al., 2007; Santos et al., 2010) in lame dairy cows. Possible reasons for their conflicting findings include the facts that HL causing lameness differ between herds, and the timing of lameness or HL relative to reproductive events could affect reproductive outcomes differently. To fully understand how lameness affects reproductive performance, it is necessary to use data based on HL, not just on visual locomotion scoring.

Hoof horn lesions likely affect reproductive performance through an inflammatory and stress response (Dobson and Smith, 2000; Dobson et al., 2003). Inflammation resulting from HL is often accompanied by minimal to extensive horn tissue damage and is associated with elevated levels of the serum inflammatory mediator haptoglobin (Smith et al., 2010) and anti-inflammatory steroids cortisol and dehydroepiandrosterone (Almeida et al., 2008). A review by Dobson et al. (2003) showed that inflammation disrupts the normal release of hormones from the hypothalamus-pituitary-ovarian axis responsible for reproduction control and impairs proper endocrine function.

To study the effect of HL on reproductive performance in lactating dairy cows and to design appropriate intervention strategies, it is necessary to follow cows with HL throughout early lactation and the breeding period. This type of longitudinal study design allows for differentiation between the effects of chronic HL (Randall et al., 2016) and new HL on reproductive performance. Only a few studies have evaluated the association between HL and reproductive performance or provided estimates according to HL type (infectious or noninfectious) and stage of development (Collick et al., 1989; Hernandez et al., 2001; Charfeddine and Pérez-Cabal, 2017). Hoof examination during the voluntary wait period to identify specific preexisting HL can provide observational evidence for an association between HL types in early lactation and reproductive outcomes in dairy cows. In addition, hoof examination at multiple intervals may provide timely insights into when HL develop and the effect of new HL on reproductive performance in lactating dairy cows. This information could guide the design of an effective breeding management strategy for cows with preexisting HL in early lactation or those that develop new HL.

Our overarching goal was to evaluate the association between HL and reproductive outcomes in lactating dairy cows. Specific objectives were to (1) evaluate

the association between HL in early lactation and the resumption of ovarian cyclicity, interval from calving to first service, pregnancy per AI (**P/AI**), and pregnancy loss to first service; and (2) to evaluate the association between the development of HL and pregnancy at 150 DIM. We hypothesized that cows with pre-existing HL in early lactation would have delayed ovulation postpartum, fewer P/AI following first service postpartum, increased risk of pregnancy loss, extended time to pregnancy, and smaller pregnancy hazard than their healthy counterparts. We also hypothesized that cows that developed new HL would have an extended time to pregnancy and smaller pregnancy hazard than cows that remained healthy.

MATERIALS AND METHODS

Farm and Management

All experimental protocols were approved by the Institutional Animal Care and Use Committee of the University of Minnesota (protocol ID: 1611–34348A). This prospective cohort study was conducted from December 2016 to December 2017 in a commercial dairy system with a total of 10,000 lactating Jersey and crossbred cows located on 3 different sites in Minnesota. Study cows were from the transition site and housed in a cross-ventilated freestall barn; stalls were bedded with recycled sand. Barn alleys had grooved concrete flooring and were scraped 3 times per day. Cows were milked 3 times per day, fed a TMR (corn silage, alfalfa hay, and concentrates) formulated according to the NRC (2001), and had ad libitum access to water.

A combination of estrus detection and timed AI was used for fertility management in the herd. Briefly, after a 35 d voluntary wait period, the breeding protocol for the first service postpartum consisted of 3 injections of prostaglandin $F_{2\alpha}$ (Lutalyse Sterile Solution, equivalent to 25 mg of dinoprost; Zoetis, Madison, NJ) administered 14 d apart at 41 ± 3 , 55 ± 3 , and 69 ± 3 DIM. Cows' tailheads were painted daily (Detect-Her tail paint; H&W Products, Salem, OH), and removal of tail paint associated with secondary signs was used as an indication of estrus. Cows were inseminated if they were detected in estrus. Cows not detected in estrus were bred using the 5-d Cosynch-72 protocol at 81 ± 3 DIM. For this protocol, cows received an injection of gonadotropin-releasing hormone (Cystorelin, equivalent to 86 μ g of gonadorelin; Merial Ltd., Duluth, GA) followed by injections of prostaglandin $F_{2\alpha}$ 5 and 6 d later, and a final injection of gonadotropin-releasing hormone concurrently with timed AI. Cows detected to

Figure 1. Diagram of experimental procedures. FEET = evaluation of feet for hoof lesions and treatment of affected cows at 20 and 120 DIM; PD = pregnancy diagnosis; US = evaluation of ovaries by transrectal ultrasonography; PG = prostaglandin $F_{2\alpha}$.

be in estrus were inseminated on the same day and did not receive further hormonal treatments.

Study Design and Data Collection

Lactating dairy cows comprising Jerseys ($n = 1,545$) and Jersey crossbreds ($n = 94$) were enrolled in the study at 20 ± 3 DIM (**D20**). Cows were enrolled using convenience sampling as they exited the rotary parlor and were examined for HL (Figure 1). At the start of each day, a list of eligible cows at 20 ± 3 DIM was generated for each pen. A priori, it was agreed with dairy farm management that we could enroll 50% of eligible cows from that list, because that was the maximum number of animals they could guarantee would be able to remain on the study site for the duration of the study. As cows left the rotary parlor, eligible cows were sorted toward the hoof-trimming chute. Sorting commenced at the start of each pen and ended to ensure that the last cow out of the hoof-trimming chute would return with its pen mates.

At 120 ± 3 DIM (**D120**), cows were re-examined for HL. All hoof examinations were conducted in a hydraulic standup chute (Appleton Single Leg Restraint; Appleton Steel Inc., Appleton WI). Hoof examinations were completed by veterinarians who were trained by the corresponding author. Excess fecal material on cow hooves was removed using a hoof knife to facilitate visual inspection of the hooves. Lesions identified were sole hemorrhage, sole ulcer, toe ulcer, white line disease, digital dermatitis, foot rot, and other nonspecific limb conditions referred to as “injury” (Cramer et al., 2008). At the D20 evaluation, no horn was removed to evaluate the foot unless an ulcer, white line disease, or toe lesion was present. At the D120 evaluation, all feet were trimmed. Lesions other than sole hemorrhage at D20 were managed by therapeutic hoof trim and application of hoof block or topical antibiotics, depending on the HL type and according to standard farm procedures. Lesions identified were recorded using an electronic hand-held device (mesa; Juniper Systems, Logan, UT),

that ran PocketTrimmer (Valley Agricultural Software, Tulare, CA), and data were synced with the farm computer, which was equipped with DairyComp 305 herd management software (Valley Agricultural Software).

Cows were evaluated for BCS at D20 and D120 using a scale of 1 to 5 described by Edmonson et al. (1989). Cows were subjected to transrectal ovarian ultrasonography using Ibex lite ultrasound equipment (E.I. Medical Imaging, Loveland, CO) on 27 and 41 ± 3 DIM to identify ovarian structures. Cows were recorded as cyclic if a corpus luteum greater than 20 mm was present in at least 1 of the ultrasound examinations.

Pregnancy Diagnosis and Calculation of Reproductive Responses

Pregnancy was diagnosed by transrectal ultrasonography on $d 34 \pm 3$ after AI. The presence of an amniotic vesicle containing an embryo with a heartbeat was used as the determinant of pregnancy. Pregnant cows were re-examined by transrectal ultrasonography on $d 62 \pm 3$ after AI. Pregnancy per AI was calculated by dividing the number of cows that were pregnant on $d 34$ and 62 by the number of cows that were inseminated. Pregnancy loss was calculated as the number of cows that lost a pregnancy between $d 34$ and 62 after timed AI divided by the number of cows diagnosed as pregnant on $d 34$ after timed AI. Cows detected in estrus before the first pregnancy diagnosis were reinseminated and considered non-pregnant from previous breeding. Data on reproductive outcomes were retrieved using the on-farm DairyComp 305 herd management software.

Statistical Analyses

Sample size calculations were conducted using the POWER procedure of SAS version 9.4 (SAS Institute Inc., Cary, NC) based on differences in P/AI observed on $d 62$ after first insemination postpartum between healthy cows and cows with HL (Santos et al., 2010). A total of 116 units per group were necessary to detect

a difference of 18 percentage points in P/AI between cows that developed a new case of hoof disease and their healthy counterparts (33.3 vs. 51.4%; $\alpha = 0.05$; $1 - \beta = 0.80$). The same number of animals per group was sufficient to depict an increase of 17.5 percentage points in pregnancy loss between healthy cows and cows with HL (Santos et al., 2010; $\alpha = 0.05$; $1 - \beta = 0.94$). Data from the herd revealed that the incidence of new cases of HL was 12%, and the rate of culling between 20 and 120 DIM was 5%. Therefore, we planned to enroll 1,250 cows in the study to allow for sufficient sample size.

Data analyses were conducted using Stata version 14.1 (StataCorp, College Station, TX). The prevalence of HL at D20 and D120 and the incidence of new HL at D120 were expressed as percentages. Because of low numbers of observations of specific HL types other than sole hemorrhage, cows with sole ulcer, toe ulcer, and white line disease were combined into a single category called “noninfectious,” and cows with digital dermatitis and foot rot into a category called “infectious.” Cows that had no identifiable HL but that expressed leg pain upon entry to the chute were recorded as “injury” ($n = 13$) and excluded from the final analysis. Cows with more than 1 HL were grouped as “multiple HL.” Cows were also divided into 3 groups based on BCS: low (≤ 2.50), moderate (2.75 to 3.25), or high (≥ 3.50). Seasons of calving were defined as fall (September to November), winter (December to February), spring (March to May), and summer (June to August).

Logistic regression models were used to evaluate the association between HL status at D20 or HL category at D20 and ovarian cyclicity, first service P/AI, and pregnancy loss. We calculated adjusted risk differences from model estimates according to the method of Norton et al. (2013). Multivariable Cox proportional hazards regression models were used to evaluate the association between HL status at D20 or HL category at D20 and interval to first service or pregnancy; in this case, the risk period was defined as the interval from enrollment to the event (first service, pregnancy, or culling). Non-pregnant animals that died or were sold before 150 DIM were right-censored. Variables included in all models were HL status, parity, BCS at enrollment, breed, and calving season.

RESULTS

Descriptive Statistics

A total of 1,639 cows were initially enrolled in this study; however, some cows were culled ($n = 120$) or moved ($n = 316$) to another site before hoof re-ex-

amination at D120. Thus, only 1,203 cows—including primiparous ($n = 773$), second lactation ($n = 144$), and multiparous ($n = 286$)—were available for statistical analyses. Table 1 shows the HL prevalence at D20 and D120 according to parity, season of calving, breed, and BCS. Overall, 26.9 and 68.4% of cows had HL at D20 and D120, respectively. The overall prevalence of HL in cows that remained in the herd and cows that were moved to another site was 27.0% (95% CI 24.8–29.1) and 30.7% (95% CI 25.6–35.8), respectively. The greatest proportion of cows was diagnosed with sole hemorrhage at D20 and D120, followed by noninfectious and infectious HL (Table 1). Of new HL, 93% were sole hemorrhage, and of those, 46 were in 2 feet, 42.2% were in 1 foot, and 11.8% were in 3 or 4 feet. Of all cows enrolled in the study, 8.8 and 8.3% had multiple HL at D20 and D120, respectively.

For lesion status at D20, cows were categorized as healthy (cows with no HL; $n = 1,197$) or lesion (cows with HL; $n = 429$). For the lesion category at D20, cows were categorized as healthy ($n = 1,197$), hemorrhage ($n = 280$), noninfectious ($n = 113$), or infectious ($n = 36$). To assess the relationship between HL development and pregnancy, cows without HL at both D20 and D120 were categorized as healthy ($n = 308$), cows with HL at D20 and no lesions at D120 were categorized as cured ($n = 72$), cows with no HL at D20 but with HL at D120 were defined as new ($n = 597$), and cows with HL at both D20 and D120 were defined as chronic ($n = 226$). Because 93% of new HL were sole hemorrhages, cows in this category were also grouped according to the number of feet affected: 1 foot ($n = 234$), 2 feet ($n = 255$), 3 or 4 feet ($n = 66$), or chronic hemorrhage ($n = 126$). Cows with chronic hemorrhage were those diagnosed with a sole hemorrhage on any foot at both D20 and D120, irrespective of the foot affected at either time point. Of the cows with chronic sole hemorrhage, 77.7% ($n = 98$) had a sole hemorrhage in the same foot at D20 and D120, and 23.3% ($n = 28$) had a sole hemorrhage in a different foot. The proportions of cows with chronic sole hemorrhage in multiple feet at D20 and D120 were 17.5% ($n = 22$) and 54% ($n = 58$), respectively.

Ovarian Cyclicity and Hazard of First Service

At 41 DIM, 51% of healthy cows and 42% of cows with HL were cyclic, respectively. Based on HL category, 42, 42, and 37% of cows with sole hemorrhage and noninfectious and infectious HL were cyclic at 41 DIM, respectively. Cows with HL at D20 had lower odds of resuming ovarian cyclicity than healthy cows [odds ratio (OR) 0.55; 95% CI 0.43–0.72; Table 2].

Table 1. Prevalence of hoof lesions diagnosed during hoof examination at early lactation (20 ± 3 DIM, D20; $n = 1,639$) and mid lactation (120 ± 3 DIM, D120; $n = 1,203$) in Jersey cows according to parity, season of calving, and BCS

Item	Early lactation/enrollment				Mid lactation/trimming			
	Healthy, % (no.)	Hemorrhage, % (no.)	Noninfectious, % (no.)	Infectious, % (no.)	Healthy, % (no.)	Hemorrhage, % (no.)	Noninfectious, % (no.)	Infectious, % (no.)
Overall	73.6 (1,197)	17.2 (280)	7.0 (114)	2.2 (36)	31.6 (380)	60.0 (720)	6.7 (80)	1.7 (20)
Parity								
1	82.9 (783)	16.1 (152)	0.6 (6)	0.0 (0)	33.6 (260)	64.8 (501)	1.2 (9)	0.3 (2)
2	71.4 (175)	15.5 (38)	8.9 (22)	2.9 (7)	29.2 (42)	56.9 (82)	6.9 (10)	6.3 (9)
3+	53.1 (239)	20.0 (90)	18.9 (85)	6.4 (29)	27.3 (78)	47.9 (137)	21.3 (61)	3.2 (9)
Season								
Fall	75.5 (115)	11.8 (18)	5.9 (9)	6.6 (10)	46.6 (55)	43.2 (51)	10.2 (12)	0.0 (0)
Spring	74.3 (304)	14.7 (60)	8.6 (35)	1.2 (5)	40.9 (111)	51.3 (139)	7.4 (20)	0.4 (1)
Summer	65.9 (230)	24.9 (87)	6.9 (24)	1.4 (5)	38.1 (90)	47.5 (112)	9.3 (22)	4.2 (10)
Winter	75.2 (548)	15.8 (115)	6.2 (45)	2.2 (16)	21.5 (124)	72.3 (418)	4.5 (26)	1.6 (9)
BCS at D20								
Low	54.9 (101)	18.5 (34)	16.3 (30)	8.2 (15)	33.9 (39)	46.1 (53)	13.0 (15)	6.1 (7)
Moderate	74.1 (995)	17.7 (238)	6.0 (81)	1.4 (19)	32.0 (324)	60.5 (612)	6.23 (63)	1.1 (11)
High	89.3 (100)	7.1 (8)	1.8 (2)	1.8 (2)	22.4 (17)	72.4 (55)	2.6 (2)	2.6 (2)
Breed								
Jersey	73.2 (1,131)	17.2 (266)	6.5 (101)	2.2 (34)	31.4 (354)	60.2 (680)	6.6 (74)	1.6 (18)
Crossbred	70.2 (66)	14.9 (14)	12.8 (12)	2.1 (2)	35.1 (26)	54.1 (40)	8.1 (6)	2.7 (2)

Similarly, irrespective of HL category at D20, cows with sole hemorrhage, noninfectious HL, or infectious HL had lower odds of cyclicity than healthy cows (Table 2).

Median time to first service was longer in cows with HL than in healthy cows (58 vs. 51 d). Based on HL category at D20, median times to first service were 56,

69, and 65 d for cows with sole hemorrhage and non-infectious and infectious HL, respectively. The proportions of cows receiving first insemination were 93 and 86% for healthy cows and cows with HL, respectively. Based on HL category, 90, 78, and 69% of cows with sole hemorrhage and noninfectious and infectious HL

Table 2. Final logistic regression model for the association between hoof lesions at early lactation (D20) and ovarian cyclicity as determined by ultrasound examinations at 27 ± 3 and 41 ± 3 DIM in Jersey cows

Item	Risk of cyclicity, %	Ovarian cyclicity			
		Adjusted risk difference	Odds ratio	95% CI	P-value
Lesion status at D20 ¹					
Healthy	50.7	Referent	Referent	—	—
Lesion	42.1	13.6	0.55	0.43–0.72	<0.001
Lesion category at D20 ¹					
Healthy	50.7	Referent	Referent	—	—
Hemorrhage	42.4	10.5	0.63	0.46–0.85	0.003
Noninfectious	42.4	10.8	0.43	0.27–0.68	<0.001
Infectious	36.7	11.0	0.37	0.16–0.82	0.014
Parity					
1	42.4	Referent	Referent	—	—
2	55.4	11.1	1.96	1.40–2.74	<0.001
3+	59.4	10.5	2.85	2.12–2.82	<0.001
Season of calving					
Winter	43.5	Referent	Referent	—	—
Fall	47.3	10.7	1.36	0.91–2.03	0.13
Spring	47.6	11.0	1.26	0.96–1.66	0.08
Summer	59.5	10.8	1.86	1.40–2.46	<0.001
BCS at D20					
Moderate	48.4	Referent	Referent	—	—
High	62.8	10.6	1.76	1.13–2.77	0.01
Low	39.6	10.8	0.49	0.33–0.72	<0.001
Breed					
Jersey	48.5	Referent	Referent	—	—
Crossbred	46.5	10.6	0.77	0.48–1.21	0.26

¹Model included parity, season of calving, breed, and BCS at enrollment. D20 = 20 ± 3 DIM.

Table 3. Multivariable Cox proportional hazards model for the association between hoof lesions and hazard of first service in lactating Jersey cows

Item	Risk of first service, %	First-service, hazard ratio	95% CI	P-value	Adjusted median interval to first service, d
Lesion status at D20 ¹					
Healthy	38.3	Referent	—	—	51
Lesion	37.2	0.81	0.71–0.91	0.001	58
Lesion category at D20 ¹					
Healthy	38.3	Referent	—	—	51
Hemorrhage	37.9	0.90	0.78–1.03	0.14	56
Noninfectious	40.9	0.66	0.52–0.83	<0.001	69
Infectious	16.7	0.58	0.38–0.87	0.01	65
Parity					
1	38.5	Referent	—	—	—
2	35.9	0.84	0.72–0.97	0.02	NA ²
3+	37.9	0.76	0.66–0.87	<0.001	NA
BCS at D20					
Moderate	38.4	Referent	—	—	—
High	36.6	1.19	0.91–1.37	0.3	NA
Low	34.6	0.56	0.46–0.67	<0.001	NA
Breed					
Jersey	38.0	Referent	—	—	—
Crossbred	36.9	1.03	0.83–1.29	0.78	NA

¹Model included parity, season of calving, breed, and BCS at enrollment. D20 = 20 ± 3 DIM.

²NA = not applicable.

were inseminated, respectively. Hazard of first service was lower [hazard ratio (**HR**) 0.81; 95% CI 0.71–0.91] in cows with HL at D20 than in healthy cows (Table 3). Cows with noninfectious and infectious HL also had a lower hazard of first service (Table 3), but we found no evidence for a difference in hazard of first service for cows with sole hemorrhage at D20 compared with healthy cows (HR 0.90; 95% CI 0.78–1.03).

First-Service P/AI and Pregnancy Loss

The proportions of cows pregnant at 34 DIM after first service were 38 and 37% for healthy cows and cows with HL, respectively. Based on HL category at D20, 38, 41, and 17% of cows with sole hemorrhage and noninfectious and infectious HL, respectively, were pregnant at 34 DIM. Overall, when HL at D20 were grouped together, we found no evidence for a difference in P/AI at first service between healthy cows and their herd mates with HL (OR 0.97; 95% CI 0.75–1.25; Table 4). Cows with infectious HL at D20 had a reduced odds of first service P/AI (OR 0.31; 95% CI 0.10–0.93) compared with their healthy herd mates. However, the odds ratios for first service P/AI were 0.99 (95% CI 0.75–1.32) for cows with sole hemorrhage and 1.13 (95% CI 0.71–1.81) for cows with noninfectious HL.

Thirty-seven cows lost a pregnancy between 34 and 62 DIM after being pregnant to first service postpartum. Of the total number of cows that became pregnant at 34 DIM, 5% of healthy cows and 11% of cows with

an HL lost a pregnancy. Based on HL category, 10, 14, and 0% of cows with sole hemorrhage and noninfectious and infectious HL, respectively, lost a pregnancy between 34 and 62 DIM. Overall, cows with preexisting HL at D20 had a higher odds of pregnancy loss to first P/AI than healthy cows (OR 1.92; 95% CI 0.94–3.95; Table 5). The odds ratio for first service pregnancy loss to first P/AI for cows with sole hemorrhage was 2.0 (95% CI 0.90–4.46) and for cows with noninfectious HL was 1.87 (95% CI 0.56–0.22). No cases of first service pregnancy loss were observed between 34 and 62 DIM in cows with infectious HL at D20.

Hazard of Pregnancy

The median intervals from calving to pregnancy were 77 and 91 d for healthy cows and cows with HL, respectively (Figure 2). The median time to pregnancy was 88, 91, and 117 d for cows with sole hemorrhage and noninfectious and infectious HL, respectively (Figure 3). At 150 DIM, 76 and 64% of healthy cows and cows with HL were pregnant, respectively. Based on HL category, 68, 58, and 47% of cows with sole hemorrhage and noninfectious and infectious HL were pregnant by 150 DIM. Cows with HL at D20 had a smaller (HR 0.84; 95% CI 0.73–0.96) hazard of pregnancy than healthy cows (Table 6).

At 150 DIM, 75% of healthy cows and 79, 81, and 69% of cows with cured, new, or chronic HL were pregnant, respectively. The median intervals from calving

Table 4. Logistic regression model for the association between hoof lesions and first-service conception in lactating Jersey cows

Item	Risk of first-service conception, %	First-service pregnancy per AI			
		Adjusted risk difference	Odds ratio	95% CI	P-value
Lesion status at D20 ¹					
Healthy	38.3	Referent	Referent	—	—
Lesion	37.2	0.94	0.97	0.75–1.25	0.82
Lesion category at D20 ¹					
Healthy	38.3	Referent	Referent	—	—
Hemorrhage	37.9	0.44	0.99	0.75–1.32	0.99
Noninfectious	40.9	0.44	1.13	0.71–1.81	0.61
Infectious	16.7	0.44	0.31	0.10–0.93	0.04
Parity					
1	37.9	Referent	Referent	—	—
2	38.5	0.2	0.93	0.67–1.28	0.66
3+	35.9	0.2	1.02	0.78–1.34	0.86
BCS at D20					
Low	34.6	Referent	Referent	—	—
Moderate	38.4	1.0	1.22	0.82–1.81	0.33
High	36.6	0.3	1.12	0.64–1.97	0.67
Breed					
Jersey	38.0	Referent	Referent	—	—
Crossbred	36.9	0.13	0.92	0.58–1.47	0.74

¹Model included parity, season of calving, breed, and BCS at enrollment. D20 = 20 ± 3 DIM.

to pregnancy were 86, 80, 82, and 103 d for healthy cows and cows with cured, new, or chronic HL, respectively. We found no evidence for an association between new HL and hazard of pregnancy (HR 1.13; 95% CI 0.96–1.32; Table 6). Covariate-adjusted survival curves

for lesion development are shown in Figure 4. The median intervals from calving to pregnancy was 86 d for healthy cows, compared to 79, 82, 86, and 93 d for cows that developed new sole hemorrhage in 1 foot, 2 feet, 3 or 4 feet, and chronic sole hemorrhage, respectively.

Table 5. Logistic regression model for the association between hoof lesions and pregnancy loss in lactating Jersey cows

Item	Risk of first-conception pregnancy loss, %	Pregnancy loss			
		Adjusted risk difference	Odds ratio	95% CI	P-value
Lesion status at D20 ¹					
Healthy	5.2	Referent	Referent	—	—
Lesion	11.2	4.7	1.92	0.94–3.95	0.08
Lesion category at D20 ¹					
Healthy	5.2	Referent	Referent	—	—
Hemorrhage	10.5	4.9	2.0	0.90–4.46	0.09
Noninfectious	14.3	6.8	1.87	0.56–6.22	0.32
Infectious	0.0	NA ²	NA	NA	NA
Parity					
1	4.6	Referent	Referent	—	—
2	10.5	7.2	2.34	0.90–6.09	0.08
3+	9.4	6.1	1.63	0.68–3.89	0.27
BCS at D20					
Low	14.9	Referent	Referent	—	—
Moderate	6.1	7.1	0.45	0.17–1.19	0.11
High	2.7	3.0	0.16	0.02–1.44	0.10
Breed					
Jersey	6.59	Referent	Referent	—	—
Crossbred	6.45	4.1	0.74	0.16–3.45	0.70

¹Model included parity, season of calving, breed, and BCS at enrollment. D20 = 20 ± 3 DIM.

²NA = not applicable (i.e., no case of first-service pregnancy loss in cows with infectious lesions at D20 was observed).

Figure 2. Covariate-adjusted survival curve, estimated from the multivariable Cox proportional hazards model, showing the cumulative proportion of Jersey cows not pregnant according to lesion status at early lactation (20 ± 3 DIM, D20). Median interval to pregnancy for healthy cows at D20 was 77 d. Median interval to pregnancy and adjusted hazard of pregnancy ratio for cows diagnosed with hoof lesions at D20 were 91 d and 0.84 (95% CI = 0.73–0.96; $P = 0.01$). Healthy = cows with no hoof lesion at D20 ($n = 1,197$); lesion = cows with any hoof lesion at D20 ($n = 429$).

Of the total number of cows that developed new sole hemorrhage in 1 foot, 2 feet, and 3 or 4 feet, 81, 83, and 77% were pregnant by 150 DIM, respectively. We found no evidence for an association between new sole hemorrhage in multiple feet and pregnancy hazard (Table 6).

DISCUSSION

Our study is the first prospective cohort study to evaluate the association between HL and reproductive performance in lactating Jersey cows. Specifically, we compared reproductive performance in cows with HL in early lactation with that of healthy cows as a reference. We also compared the interval to pregnancy in cows that developed new HL between early and mid lactation with cows that remained healthy over the same period.

Results from our study indicate that preexisting HL in early lactation are associated with reduced odds of cyclicity and extended interval for calving to first service. We also found that the reduced odds of cyclicity were relatively consistent between the different types of HL in early lactation. Although specific HL associated with lameness were not identified in their study, Garbarino et al. (2004) found that 238 Holstein cows diagnosed as lame based on visual locomotion score during the early postpartum period also had reduced odds of

cyclicity compared with cows that were classified as healthy. Although the mechanism of reduced cyclicity in cows with HL in our study was unclear, previous studies have shown that fertility responses are lower in lame cows than in healthy cows (Hernandez et al., 2005; Walker et al., 2008). However, considering that lameness is painful and caused mostly by HL, reduced cyclicity may be attributed to an inflammatory or stress response in the hypothalamo-pituitary-gonadal axis (Dobson et al., 2003; Walker et al., 2008) that affects GnRH/LH pulsatility in the early postpartum period (Moenter et al., 1992; Morris et al., 2011). Impaired gonadotrophin-releasing hormone/luteinizing hormone pulsatility has been linked to delayed ovulation or postpartum ovulatory failure in cattle (Melendez et al., 2018). Furthermore, HL may impair normal feeding behavior and affect nutrient balance in early lactation, which could further affect resumption of ovarian cyclicity and interval to first service. Norring et al. (2014) reported that lameness was associated with changes in the feeding behavior of dairy cows in early lactation. Walker et al. (2008) also found differences in grazing bite rate between cows that were lame and cows that were not lame.

Although using a different study design, Charfeddine and Pérez-Cabal (2017) and Barkema et al. (1994) concluded that the average interval for calving to first

Table 6. Multivariable Cox proportional hazards regression models for the association between hoof lesions and hazard of pregnancy in lactating Jersey cows

Item	Risk of pregnancy, %	Pregnancy hazard ratio	P-value	95% CI	Adjusted median interval to pregnancy, d
Lesion status at D20 ¹					
Healthy	75.5	Referent	—	—	77
Lesion	63.6	0.84	0.01	0.73–0.96	91
Lesion category at D20 ¹					
Healthy	75.5	Referent	—	—	77
Hemorrhage	67.9	0.85	0.04	0.72–0.99	88
Noninfectious	57.9	0.87	0.31	0.67–1.14	91
Infectious	47.2	0.69	0.15	0.42–1.14	117
Lesion development ¹					
Healthy	75.3	Referent	—	—	86
Cured	79.2	1.26	0.13	0.94–1.69	80
New	80.9	1.13	0.14	0.96–1.32	82
Chronic	69.4	0.91	0.37	0.73–1.12	103
New hemorrhage status ¹					
Healthy	75.3	Referent	—	—	86
Hemorrhage, 1 foot	81.2	1.18	0.09	0.97–1.44	79
Hemorrhage, 2 feet	83.1	1.16	0.13	0.95–1.41	82
Hemorrhage, 3 and 4 feet	77.3	0.98	0.89	0.72–1.33	86
Chronic hemorrhage	72.2	0.97	0.81	0.76–1.24	93

¹Model included parity, season of calving, breed, and BCS at enrollment. D20 = 20 ± 3 DIM.

service was longer in lactating Holstein cows with hoof disorders. In addition, Walker et al. (2010) and Morris et al. (2011) reported reduced estrus intensity in lame

cows based on visual locomotion scores. Data from the current study show that cows with HL during the voluntary wait period had a longer interval for calv-

Figure 3. Covariate-adjusted survival curve, estimated from the multivariable Cox proportional hazards model, showing the cumulative proportion of Jersey cows not pregnant according to lesion category at early lactation (20 ± 3 DIM, D20). Median interval to pregnancy for healthy cows at D20 was 77 d. Median interval to pregnancy and adjusted hazard ratios for cows diagnosed with sole hemorrhage and noninfectious and infectious hoof lesions at D20 were 88 d and 0.85 (95% CI = 0.72–0.99; $P = 0.04$), 91 d and 0.87 (95% CI = 0.67–1.13; $P = 0.31$), and 117 d and 0.70 (95% CI = 0.42–1.14; $P = 0.15$), respectively. Healthy = cows with no hoof lesion at D20 ($n = 1,197$); hemorrhage = cows with a sole hemorrhage at D20 ($n = 280$); noninfectious = cows with a sole ulcer, toe ulcer, or white line disease at D20 ($n = 114$); infectious = cows with digital dermatitis or foot rot ($n = 36$).

ing to first service. The longer interval from calving to first service observed in the current study may be attributed to a failure to express estrus or ovulation of a low estrogenic follicle, resulting in estrus behavior of low intensity. According to the review by Dobson et al. (2008), stress associated with lameness reduces LH pulsatility required to drive estradiol production by the dominant follicle, and as a consequence results in less intense estrus behavior and failure to initiate an LH surge.

The smaller hazard of pregnancy observed in cows with HL in our study corroborated the findings of others in Holstein cows categorized as lame according to increased locomotion scores (Hernandez et al., 2005; Bicalho et al., 2007). In the study by Hernandez et al. (2005), the association between lameness severity as ascertained by visual locomotion scoring revealed that cows that were mildly and severely lame had 29 and 58% decreased hazards of pregnancy, respectively, compared with cows that were not lame. These values were greater than those reported for cows with sole hemorrhage in early lactation in our study.

To our knowledge, this is the first study to evaluate the association between the development of new HL and pregnancy hazard. We found no evidence that cows

that developed new HL had a lower pregnancy hazard. This may have been because in our study, the majority of new HL were sole hemorrhage. Sole hemorrhage is a mild and early form of more severe noninfectious HL, which are extremely painful and associated with clinical lameness (O'Driscoll et al., 2015). Nonetheless, it is possible that sole hemorrhage is associated with subclinical hoof pain and immune system activation (Flower and Weary, 2006). Considering that sole hemorrhage in early lactation was associated with smaller hazard of pregnancy in our study, emphasis should be placed on early diagnosis and management of new sole hemorrhage to reduce the prevalence of chronic cases. Early management of mild HL is essential, because cows with severe HL are less likely to recover (Leach et al., 2012; Miguel-Pacheco et al., 2017).

In the current study, the majority of animals enrolled were in their first lactation, and this raises the question of whether an intervention before calving would have been beneficial. Managing heifers to reduce severe lesions is likely to have positive herd effects (Gomez et al., 2015; Randall et al., 2016). Specifically, hoof trimming of heifers before or around first calving has been suggested to improve future performance and reduce incidence of culling. In the study by Randall et

Figure 4. Covariate-adjusted survival curve, estimated from the multivariable Cox proportional hazards model, showing the cumulative proportion of Jersey cows not pregnant according to lesion development. Median interval to pregnancy for healthy cows at early lactation (20 ± 3 DIM, D20) was 86 d. Median interval to pregnancy and adjusted hazard ratios for cows diagnosed with cured, new, and chronic hoof lesions at mid lactation (120 ± 3 DIM, D120) were 80 d and 1.26 (95% CI = 0.94–1.69, $P = 0.13$), 82 d and 1.12 (95% CI = 0.96–1.33, $P = 0.14$), and 103 and 0.90 (95% CI = 0.73–1.12, $P = 0.37$), respectively. Healthy = cows with no hoof lesion at D20 ($n = 308$); cured = cows with a lesion at D20 and no lesion at D120 ($n = 72$); new = cows with no lesion at D20 and a lesion at D120 ($n = 596$); chronic = cows with a lesion at D20 and D120 ($n = 216$).

al. (2016), heifers with severe hoof horn lesions had an increased risk of future lameness. However, in another study, Mahendran et al. (2017) did not observe a beneficial effect of a pre- or post-calving hoof-trimming regimen on subsequent lameness episodes in Holstein heifers. Nonetheless, the effect of the hoof-trimming technique and specific HL types on the future health and lifetime productivity of dairy heifers requires further investigation.

The overall prevalence of HL in our study was within the range reported for Jerseys (Chawala et al., 2013) and Holsteins (Manske et al., 2002; Hernandez et al., 2005; Cramer et al., 2008). In our study, sole hemorrhage was the most commonly observed HL in both early and mid lactation. A greater prevalence of digital dermatitis compared with other HL has been reported by others (Cramer et al., 2008; Solano et al., 2016). These differences in the prevalence of specific HL may be the result of housing hygiene conditions, flooring system, genetics, hoof management routine, footbath practices, and length of distance cows are required to walk each day (Cook et al., 2004; Solano et al., 2016).

A limitation of this study was a rate of occurrence of severe HL such as sole ulcer, white line disease, digital dermatitis, and foot rot that was lower than expected, necessitating the collapse of severe hoof diseases into categories (noninfectious and infectious HL). As a result, we were unable to evaluate associations for specific HL. The finding that more cows with HL were moved to different sites could also have influenced our estimates. Although we took steps to mitigate the possibility of this occurring during protocol development with the participating dairy, it was not possible to completely eliminate the movement of study cows. We expected a certain amount of cow movement and therefore enrolled more cows than our sample size calculation required.

Furthermore, hemorrhage scoring in the current study was limited in that it did not differentiate between diffused or circumscribed hemorrhage. In addition, animals in the current study were managed using reproductive hormones to induce estrus and synchronize ovulation. These interventions could have modified fertility responses in cows with HL. The majority of the HL in our study were sole hemorrhage, and the diagnosis of sole hemorrhage has been shown to vary between hoof trimmers (Cramer et al., 2008; Holzhauer et al., 2006). Furthermore, at D20 no horn was removed, restricting the diagnosis of cows with hemorrhage to those that had hemorrhage for a longer period. At present, there is no way to determine the presence of hemorrhage in deeper layers of the horn without hoof trimming. This inherent lag in the time of outcome means that we likely underdiagnosed the

presence of hemorrhage at D20 and overestimated the development of new sole hemorrhage. This is another possible explanation for the lack of evidence of an association between new HL and reproductive outcomes. Because cows with preexisting HL had an extended interval to first service and smaller pregnancy hazard by 150 DIM, further research to evaluate the effects of timed AI programs on the reproductive performance of cows with HL in early lactation is recommended. Instituting a program that targets the routine identification of cows with HL during the voluntary wait period will be useful in identifying cows that are likely to benefit from such targeted reproductive management.

CONCLUSIONS

Compared with healthy cows, cyclicity was reduced in cows with HL in early lactation, irrespective of lesion type. Also, cows with noninfectious and infectious HL in early lactation had a smaller hazard of first service than healthy cows. Cows with sole hemorrhage in early lactation had a smaller pregnancy hazard than healthy cows. We found no evidence for differences in pregnancy hazard between healthy cows and those that developed new HL. Future efforts should focus on strategies to minimize the occurrence of HL in early lactation in dairy cows and evaluate targeted reproductive management for cows with HL in early lactation.

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