The influence of early postpartum uterine and ovarian recovery status on subsequent reproductive performance in Holstein dairy cows

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SUMMARY

Examination of uterine involution and ovarian cycle resumption at approximately one month postpartum in dairy cows and treatment interventions based thereon are widely performed; however, it has not been clearly demonstrated whether doing so improves the profitability of farms. One reason for this is that current reproductive examinations by rectal palpation and ultrasonography depend heavily on veterinarian knowledge, skills, and experience. If there are simpler and objective diagnostic criteria for these examinations, it might be possible to increase the cost-effectiveness of early postpartum reproductive examinations. Therefore, we aimed to establish suitable diagnostic criteria based on relatively simple findings for the uteri and ovaries through these examinations. A total of 4,912 Holstein Friesian cattle subjected to reproductive examinations between 28 and 45 days postpartum were examined at 12 dairy farms conducting regular reproductive examinations. The uteri were divided into three groups based on the diameter of the gravid uterine horn: Small, < 30 mm; Medium, ≥ 30 mm; and Large, ≥ 30 mm, with pus retention. Ovaries were classified into four groups: heat (HT); corpus luteum (CL); no structure (NS); and ovarian cyst (OC). The incidence in each group was examined. The number of days from calving to conception (days open) for cows was analyzed using Kaplan-Meier survival analysis. As a result, the incidence rates for all of the tested cattle were 48.1% in the Small group, 45.3% in the Medium group, and 6.6% in the Large group, with the median days open being 107 days, 118 days, and 205 days for each group, respectively, with significant differences observed between each group. Going by ovary classifications, the figures were 10.9% for the HT group, 51.3% for the CL group, 20.6% for the NS group, and 17.2% for the OC group, with the median days open being 98, 104, 126, and 149, respectively. The number of open days was significantly shorter in the HT group than in the other groups. Upon combining three groups of uterine and four groups of ovarian statuses and then dividing them into 12 groups, the days open was especially prolonged in the Large-CL, Large-NS, and Large-OC groups. The Large-CL group showed a significant increase in days open, even when compared with all the groups in the Medium and Small groups. The shortest days open was found in the Small-HT group, which was significantly shorter than all the other groups except the Medium-HT group. Based on the findings for the uteri and ovaries in the reproductive examinations performed 28-45 days postpartum, it was suggested that it would be possible to improve productivity by selecting cows who are likely to have extended days open and by appropriately applying treatment interventions.

KEY WORDS

Days open; reproductive examination; uterine involution; resumption of ovarian cyclicity.

INTRODUCTION

One of the causes of poor reproductive performance in dairy cows is delayed genitalia recovery postpartum or, in other words, delayed uterine involution and resumption of ovarian cyclicity (1). To improve this, the practice of reproductive examination approximately one month postpartum and treatment interventions based thereon have been implemented in commercial dairy herds since the 1980s, and the practice is now widespread. Treatment interventions include administering medication to individual cattle and improving herd management techniques (2). However, there is no evidence to date that examinations and interventions improve farm profitability, and some even argue that they should be discontinued because they are not cost-effective (3).

This early postpartum reproductive examination is intended to improve productivity; therefore, all targeted cows should be examined quickly and at a low cost, and the results should be available immediately. Accordingly, in the current situation, early postpartum examinations are mainly performed using rectal palpation and ultrasonography. Therefore, the accuracy of the diagnosis and appropriateness of the choice of treatment method depends largely on the knowledge, skills, and experience of the individual veterinarian. If there were simpler and

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more objective diagnostic criteria and guidelines for determining prognoses in these examinations, the gaps in knowledge and experience of the veterinarians could be bridged, and cost-effectiveness could be increased.

Therefore, to create useful evaluation criteria for use in the field, we examined the uterine and ovarian status obtained during early postpartum reproductive examinations and analyzed the relationship with calving-to-conception interval (days open).

MATERIALS AND METHODS

Farms and animals

A total of 4,912 Holstein Friesian cattle calved between January 1, 2014 and December 31, 2016 at 12 commercial dairy farms that conducted regular herd check programs were investigated. The scale of farm rearing was 80 to 500 cattle, the type of rearing was a free-stall barn and milking parlor, and the feeding was *ad libitum* total mixed ration. The average annual milk production per cow was approximately 10,700 kg, and the reproductive performance was 15 to 24% for the pregnancy rate and 102 to 141 days for the average days open (Table 1).

Experimental design and rectal examinations

Cows were subjected to rectal palpation and ultrasonography at 28-45 days postpartum to determine the recovery status of the uteri and ovaries and the subsequent days open. All cows were studied at each farm, except for cows scheduled to be culled because of low milk yield, poor milk quality, old age, and other reasons. The voluntary waiting period was set to 55 to 60 days (4), after which heat detection and artificial insemination (AI) were actively performed. Treatment was administered as needed after 46 days postpartum in cows with reproductive disorders, such as follicular cysts and endometritis. Heat induction and timed AI were also performed in anestrus cows. For cows that had not conceived for an extended period, it was judged that breeding should stop upon request from the owner.

Pregnancy was diagnosed three times at 28-44 days, 55-78 days, and 180-210 days post-insemination using rectal palpation and ultrasonography. Pregnancies that continued beyond 150 days of gestation were considered to have achieved conception, while those that were miscarried before 150 days were considered unconceived. For the ultrasonic imaging devices, 7.5 MHz sector probes Tringa 50s (Esaote Pie Medical, Maastricht, Netherlands) or Easy-scan (BCF Technology, Scotland, UK) were used.

Uterus

The diameter of the base of the gravid uterine horn was measured by rectal palpation and ultrasonography, and the presence of pus retention in the uterus was recorded. For uterine diameter, the diagnostic criteria were created with reference to the uterine involution curve for Holstein Friesian cattle from Zhang et al. (5) and Lin et al. (6). In both reports, differences were observed in the diameter of the gravid uterine horn immediately after calving, depending on parity, but no differences were observed at 28 days postpartum. In addition, Lin et al. (6) reported that the number of days for uterine horns to return to their original diameter in primiparous cows was 29.5 days postpartum with a diameter of 30.4 mm, 30 days postpartum, and 31 mm in biparous cows, and 27.1 days postpartum and 31.5 mm for multiparous cows. In this study, since the first examination was performed 28-45 days postpartum, different diagnostic criteria for the diameter of the uterus depending on parity were not established, with uniform criteria used regardless of parity.

The cows were categorized into three groups: a small group comprising cows with a uterine horn diameter of less than 30 mm at 28 to 45 days postpartum; a medium group comprising cows with a uterine horn diameter of 30 mm or more but no pus retention in the uterus; and a large group comprising cows with a uterine horn diameter of 30 mm or more and pus retention in the uterus. The cows in each group were examined, and the number of open days was compared.

In the Small and Medium groups, cows that had undergone some treatment intervention 28-45 days postpartum were excluded from the days open comparison. In the Large group, cows

Table 1 - Farm information in the experiment period, from 2014 to 2016.

Farm	Scale of the dairy farm (heads)	Total number of dairy cows used in this experiment (heads)	Average milk produciton per cow (kg/305 days)	Average pregnancy rate (%)	Average days open (days)	Location in Japan (prefecture)
1	110	321	11290	17	114	Ibaragi
2	130	381	10490	15	126	Okayama
3	400	1231	11590	28	102	Tokushima
4	65	190	10065	19	119	Tottori
5	120	312	11285	21	120	Tottori
6	60	190	10370	20	138	Tottori
7	60	152	11895	22	104	Tottori
8	140	401	10070	19	120	Tottori
9	150	442	9820	16	127	Tottori
10	150	399	10680	15	135	Mie
11	120	351	10420	21	127	Mie
12	500	542	10350	17	121	Ehime

that had undergone treatment intervention at the time of the examination were included in the days open comparison. The reason for this was that the Large group was composed of cows that had retained pus in the uterus, and it was disadvantageous for farmers to leave such conditions untreated, which would also be a problem from the viewpoint of the animal's welfare. Therefore, no separate treatment groups were established. The treatment interventions for the Large group comprised 25 mg of PGF_2 (dinoprost tromethamine, Pronargon F injection for animals, Zoetis Inc., Tokyo, Japan), which was administered intramuscularly.

Ovary

The structures of the ovaries were examined by rectal palpation and ultrasonography and classified into the following four conditions in accordance with the uterine contraction status, structure, and other external indications. Heat (HT) group: cows with follicles 14-22 mm in diameter that can be ovulated (7), or where there is evidence of them having ovulated, with strong uterine contractions (8), and that often have estrus mucus or post-estrus bleeding from the vulva. Ultrasonography often reveals hypoechoic fluid retention in the uterus, intimal thickening, and inhomogeneous structures in the uterus (9), which are thought to be both pre- and post-heat. Cows were classified into the HT group even if they had large follicles or follicular cyst-like structures >22 mm in diameter along with urine contraction or individual follicles of a size that could be ovulated and if there were other symptoms of heat. The corpus luteum (CL) group consisted of cows with CL of 20 mm or more in diameter and those with so-called CL-like structures with a CL tissue thickness equal to or greater than 3 mm (10). A slight tone was observed in the uterus. No structure (NS) group: cows without follicles or CL, with small follicles only, less than 8 mm; those without CL and with follicles of 8 mm or more but less than 25 mm, but with a flaccid uterus and no other signs of heat, and judged not to be in heat (11). Ovarian cyst (OC) group: cows without CL, a flaccid uterus, follicular cyst-like structures equal to or greater than 25 mm in diameter and less than 3 mm in cyst wall thickness, or multiple follicles equal to or greater than 18 mm in diameter (11).

We examined the number of cows in the four groups and compared the number of open days. In this comparison, to objectively determine the effect of ovarian function on the days open, those cows that had undergone some treatment intervention at the time of the examination 28 to 45 days postpartum were excluded.

Combinations of uterus and ovary

The findings of three uterine groups (Small, Medium, and Large) and four ovarian groups (HT, CL, NS, and OC) were combined into 12 groups, and the number of animals in each group was examined and the days open compared. In this comparison, cows that had undergone some treatment intervention at the time of the examination between 28 and 45 days postpartum were excluded from the days' open comparison; however, those cows in the Large group that had undergone treatment intervention at the time of examination were included in the comparison.

Statistical analysis

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) (12), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). Kaplan-Meier survival curves were plotted to compare days open, with significant differences verified using the log-rank test. In this study, the event was defined as "conception," and the start of observation was calving. The median number of days open is shown as a representative value for each Kaplan-Meier curve. The date on which the observations were censored was when the cow was decided to be culled or the day of culling. Dairy Comp 305 (Valley Agricultural Software, Tulare, CA) was used for data management of individual cattle.

RESULTS

Days open in the status of the uterus and ovary

All cows were examined and the number of cows in each group is shown in Table 2. For the uterus, the Small and Medium groups accounted for more than 90% of the total, with the Large group, which had the slowest uterine involution and in which there was a retention of pus in the uterus, accounting for 323 cows (6.6%). In terms of the ovarian findings, the CL group had the highest number of cows, at 2,520 (51.3%). In addition, of the 323 cows in the Large group that had pus retention in the uterus, 90% or more were in the CL group, and none were in the HT group. In the uterine groups, the median number of days open in the Small (n = 1558), Medium (n = 793), and Large (n = 323) groups were 107, 118, and 205 days, respectively, with significant differences observed across all groups in the log-rank test (P<0.01) (Figure 1).

Table 2 - Number and ratio of dairy cows used in this experiment. Findings of the uterus were divided into three groups (Small, Medium, and Large), and of the ovary were divided into four groups: heat (HT); corpus luteum (CL); no structure (NS); and ovarian cyst (OC) at reproductive examination in 28-45 days postpartum. The figures in parentheses refer to the numbers of cow in comparison with the days from calving to pregnancy (the days open) by Kaplan-Meier survival analysis.

		Ovary*			
		HT,	CL,	NS,	OC,
		535, 10.9% (477)	2520, 51.3% (1133)	1010, 20.6% (636)	847, 17.2% (105)
Uterus*	Small, 2362, 48.1% (1558)	427	1138	423	374
	Medium, 2227, 45.3% (793)	108	1087	568	464
	Large, 323, 6.6% (323)	0	295	19	9

*Size of the uterus and status of the ovary were defined using our standards, and data of the standards are explained in the Materials and Methods section.

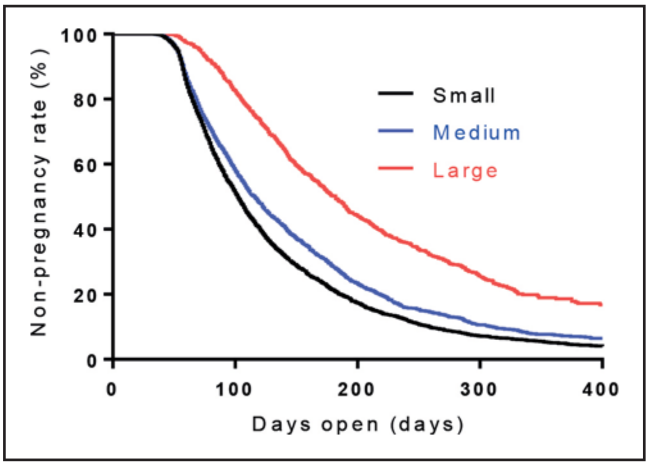

Figure 1 - Kaplan-Meier survival analysis for days open according to the size of the uterus. Log-rank test revealed statistically significant differences between groups (p < 0.01). Cows were divided into three groups according to the diameter of the gravid uterine horn as follows: Small, <30 mm; Medium, ≤30 mm; Large, ≤30 mm, with pus retention in the uterine cavity. The number of cows and median days open in each group were as follows: Small, 1,558 cows and 107 days; Medium, 793 cows and 118 days; Large, 323 cows and 205 days.

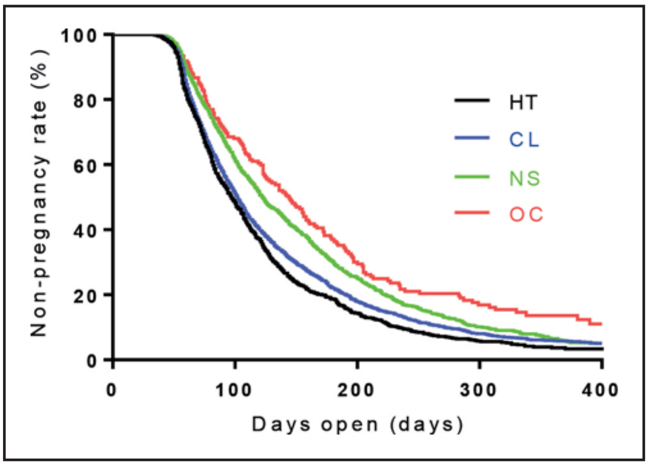

Figure 2 - Kaplan–Meier survival analysis for days open according to the status of the ovary. Log-rank test revealed the significant differences between groups (p < 0.01, except NS vs OC). Ovaries were divided into four groups according to the status of the ovary as follows: heat (HT); corpus luteum (CL); no structure (NS); and ovarian cyst (OC). The number of cows and median days open in each group were as follows: HT, 477 cows and 98 days; CL, 1,133 cows and 104 days; NS, 636 cows and 126 days; OC, 105 cows and 149 days.

The median number of days open in the four groups classified by ovarian findings was 98 for the HT group (n = 477), 104 for the CL group (n = 1133), 126 for the NS group (n = 636), and 149 for the OC group (n = 105); the HT group was significantly shorter than the other three groups in the log-rank test ($P < 0.01$) (Figure 2). The CL group's days open was significantly longer ($P < 0.01$) than that of the HT group, and significantly shorter than that of the NS and OC groups ($P < 0.01$). No significant differences were observed between the NS and OC groups.

Days open in the combination of the uterus and ovary

The median number of days open and significant differences between the 12 groups according to the combination of uterine and ovarian findings are shown in Table 3. The number of days open was especially prolonged in the Large-CL, Large-NS, and Large-OC groups. The Large-CL group showed a significant increase in days open, even when compared with all the groups in the Medium and Small groups. The Medium-NS and Medium-OC groups had prolonged days open. These were significantly longer than the Medium-HT and Medium-CL groups and most of the Small groups. The shortest days open was in the Small-HT group, which was significantly shorter than all groups except the Medium-HT group.

DISCUSSION

This study was conducted on almost all parturient cows on 12 medium-scale commercial dairy farms. Therefore, we did not target a select group of cows. We studied a variety of cows in terms of management factors, parturition stress, fulfillment of nutritional requirements, and periparturient diseases. Regarding the recovery of the cows' reproductive organs, it is likely that the data reflects the overall picture of Holstein Friesian cows in Japan.
In the comparison of days open by uterine findings, the Small

Table 3 - Days from calving to pregnancy (days open) of the dairy cows used in this experiment. The cows that were treated in 28-45 days postpartum were excluded from the comparison, except the large uterus group. Kaplan-Meier survival analyses and log-rank tests were performed to compare statistical differences between the groups.

		Small				Medium				Large		
		HT	CL	NS	OC	HT	CL	NS	OC	CL	NS	OC
Number of cows (heads)		393	754	356	55	84	379	280	50	295	19	9
Median period of open (days)		97	102	120	114	101	106	144	184	202	276	214
Small	HT		<0.05	<0.01	<0.05	NS	<0.05	<0.01	<0.01	<0.01	<0.01	<0.01
	CL			NS	NS	NS	NS	<0.01	<0.01	<0.01	<0.01	<0.05
	NS				NS	NS	NS	<0.01	<0.01	<0.01	<0.01	<0.05
	OC					NS	NS	NS	<0.05	<0.01	<0.01	<0.05
Medium	HT						NS	<0.01	<0.01	<0.01	<0.01	<0.05
	CL							<0.01	<0.01	<0.01	<0.01	<0.05
	NS								NS	<0.01	<0.01	NS
	OC									<0.05	NS	NS
Large	CL										NS	NS
	NS											NS
	OC											

HT, heat; CL, corpus luteum; NS, no structure; OC, ovarian cyst; NS, not significant.

group showed the shortest days open, followed by a significantly longer days open in the Medium group. Although the Large group comprised only a small number of cows, at 6.6 % of the total, the days open was 205 days, a significantly longer number of days than the other groups. From these results, it is strongly suggested that it is possible to determine the days open using the simple criterion of determining whether the gravid uterine horn diameter was larger or smaller than 30 mm and then confirm if there was pus retention in the uterine cavity at 28 to 45 days postpartum. Furthermore, pus retention in the uterus was strongly linked to prolonged days open.

Regarding the ovarian findings, the HT and CL groups considered as having resumed ovarian cyclicity accounted for approximately 60% of the total. The existence of the CL between 28 and 45 days postpartum indicates that the CL was formed after ovulation. The NS and OC groups, which account for approximately 40%, are considered anovular, where ovarian cyclicity has not yet resumed (13). The number of open days was shorter in the HT and CL groups and longer in the NS and OC groups. This is consistent with a number of reports showing that early first ovulation reduces the number of days open, while delayed first ovulation prolongs the number of days open (14, 15). It has been reported that the average number of postpartum days until the first ovulation is 29.7, but the mode is 18 (16), indicating that the presence of cows with an extremely late first ovulation may increase the average number of days until the first ovulation (17).

The NS and OC groups in this study may have included such cows, and detecting and taking measures against such cows, which account for nearly 40% of the number of cows, may be of great significance in improving the reproductive performance of an entire farm.

Cattle that had undergone treatment intervention at the time of examination (i.e., the Large group) were excluded from the comparison of the four ovarian groups. Since the effects of uterine diseases were greater in the Large group and an extreme prolongation of the days open was observed, the impact of the ovarian findings on the days open could be more purely evaluated through exclusion. However, the classification of the ovaries in this study was based on a single examination. According to a single ultrasound examination, the sensitivity and specificity of diagnosing CL were 91.4 to 96.7% and 100% (18), respectively; the sensitivity and specificity of diagnosing anovulation were 85.7% and 87.7% (19), respectively, and the sensitivity and specificity of making a differential diagnosis of follicular cysts from luteal cysts were 86.7% and 82.3% (20), respectively. Some ovarian cysts stop steroid secretion and no longer prevent the resumption of the ovarian cycle (21, 22). The classification of ovarian status using the method used in this study can be performed quickly and at a low cost, with results available immediately. Therefore, we believe that this is practical because it is consistent with the purpose of performing early postpartum reproductive examinations.

The Large-HT group had zero cows, with most of the Large group having CL. This may be because the production of PGF_2 in the endometrium was inhibited by uterine diseases, such as pyometra and purulent endometritis indicated by retention of pus in the uterus, resulting in a persistent CL (23). In addition, a significant prolongation in the days open was observed despite treatment intervention with intramuscular administration of PGF_2, suggesting that an improvement in the treatment method is necessary.

Cows with delayed recovery in both the ovary and uterus were classified into the Medium-NS or Medium-OC groups, showing the longest days open after the Large group. Periodic changes in sex hormones due to the recovery of ovarian cyclicity are known to promote uterine involution (24). Also, it has been reported that LPS from bacteria in the uterus negatively affects the recovery of ovarian cyclicity (25). In other words, since the recovery of the ovaries and uterus are thought to be closely related to each other, reproductive performance in these two groups may be improved by providing some initial treatment intervention for the ovaries and/or uterus at the time of examination.

In the Small-HT, Medium-HT, and Small-CL groups, the median number of days open was around 100, shorter than the targeted 115 days (26) for reproductive performance, suggesting that recovery of the reproductive organs was better for cows classified into these groups, and that reproductive performance would be good even without active treatment intervention. However, there was a significant difference between the days open in the Small-HT group (98 days) compared with the Small-CL group (104 days) and the Medium-CL group (106 days). It may be that the Small-CL and Medium-CL groups included cows with CL and related uterine diseases, particularly subclinical endometritis (27, 28).

CONCLUSIONS

In conclusion, in the reproductive examination at 28 to 45 days postpartum, cows exposed to heat had the shortest days open. The number of days open in individuals with CL but no pus retention in the uterus was shorter than the general criteria, suggesting that there was no particular need for early intervention. Cows with delayed recovery in both the uterus and ovary, that is, cows with a uterine horn diameter of 30 mm or more and ovaries with NS or follicular cysts, had prolonged days open. Therefore, it might be possible to shorten the number of open days by performing treatment interventions. Since those with pus retention in the uterus had the longest open days, more proactive treatment intervention is necessary. Based on the findings for the uterus and ovaries in the reproductive examination performed 28-45 days postpartum, it is possible to select individuals who are likely to have extended days open and provide them with treatment interventions accordingly.

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