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Role of mastitis in on-farm deaths of Finnish dairy cows

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ABSTRACT

According to our recent necropsy-based study, mastitis is the most common underlying diagnosis of on-farm deaths in Finnish dairy cows. However, it remained unanswered to what extent mastitis has contributed to death of all necropsied cows. In the present study, based on histopathology, we detected one-third of the necropsied dairy cows having active inflammatory udder lesions ($n = 110$). The role of mastitis varied and was interpreted by causes of death (underlying, intermediate, immediate, other significant). Mastitis was most commonly the underlying (28%) or both immediate and underlying cause of death (48%), and only seldom was it the immediate (4%) or intermediate (4%) cause of death. Mastitis occurred either as the only cause leading to death (mastitis only, MO; 39%), or with many other contributing diseases (multiple diseases, MD; 61%), which were interacting with mastitis and together leading to death. Between these groups (MO vs. MD), time of mastitis occurrence during lactation, producer-reported duration of illness, clinical signs, and medication differed, as well the histopathologic severity of mastitis. The cases where mastitis was the only initial insult occurred evenly throughout the entire lactation, but the cases with many interacting diseases were clustered in early lactation. In MD cows, cases of mastitis occurred concurrently with metritis (31%), aspiration pneumonia (24%), acute trauma or dystocia (15%), or with other diseases, such as ketosis, hepatic lipidosis, rumenitis, and abomasal diseases. For a pathologist, the gross mastitis diagnosis was most challenging at the beginning of the lactation, especially if inflammation was mild to moderate, suggesting the value of histopathologic examination being highest at that time. Also, producers reported mastitis signs less frequently if cow had many simultaneously occurring diseases. Therefore, even if clinical signs of

other diseases are present, the udder should be considered a potential cause of illness and should be examined, especially in dry and transition-period cows.

Key words: dairy cow, mastitis, on-farm death, necropsy, histopathology

INTRODUCTION

Mastitis is the most common and costly disease of dairy cows, with incidence ranging from 21.9 to 24.4 per 100 cow years (Olde Riekerink et al., 2008; Fukushima et al., 2020; Gonçalves et al., 2022). High-yielding older cows are most susceptible to mastitis (Valde et al., 2004; Olde Riekerink et al., 2007; Niemi et al., 2021). Because of its common occurrence, mastitis causes substantial financial losses for the dairy industry. Losses for producers accrue from veterinary and treatment costs, decreased milk yield, discarded milk, mastitis prevention procedures, and culling of diseased cows (Heikkilä et al., 2012; Aghamohammadi et al., 2018). Estimated costs of clinical mastitis have ranged from €240 to €485 per case (Heikkilä et al., 2012; van Soest et al., 2016), demonstrating the considerable negative impact on dairy farm profitability.

Mastitis can be classified as subclinical or clinical, the latter being either peracute, acute, subacute, or chronic (Egyedy and Ametaj, 2022). Clinical mastitis is a painful disease that can compromise animal welfare and lead to death, although the fatality rate is generally low (Seegers et al., 2003). However, in severe mastitis cases, mortality can increase up to one-third (Krebs et al., 2023), and cows with clinical mastitis also have higher probability of being culled (Bar et al., 2008; Haine et al., 2017). Clinical mastitis often occurs at the beginning of the lactation (Bar et al., 2008; Olde Riekerink et al., 2008; Gonçalves et al., 2022), sometimes together with other common transition-period diseases, such as hypocalcemia and ketosis (Curtis et al., 1985; Bar et al., 2008). Only a few studies, however, report how frequently these diseases occur together or predispose one to the other (Curtis et al., 1985; Correa et al., 1993; Pinedo et al., 2010).

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The list of standard abbreviations for JDS is available at adsa.org/jds-abbreviations-24. Nonstandard abbreviations are available in the Notes.

Postmortally, mastitis is determined as an inflammatory reaction in the mammary gland, and definite diagnosis can be achieved through histopathology. Histopathology of mastitis is well described in experimental (Helmboldt et al., 1953; Frost and Brooker, 1986; Trinidad et al., 1990) and naturally occurring mastitis (Benites et al., 2002; Bianchi et al., 2019; Leitner et al., 2020), but no studies have described if these cows have had mastitis signs at the time of death or euthanasia. Additionally, the role of mastitis in on-farm deaths is not well known, because only one 40-yr-old retrospective necropsy-based study has focused on cows that died or were euthanized due to mastitis (Hazlett et al., 1984).

The cause of death can be either underlying, intermediate, immediate, or other significant (McConnel and Garry, 2017). An underlying cause of death is a disease or an injury that initiates the causal chain reaction leading to death. An intermediate cause of death is a consequence of an underlying cause, and at times, multiple intermediate causes may exist. They end up with the immediate cause of death, which is the final outcome just before a cow's death or euthanasia (McConnel et al., 2010). Other significant or contributing causes of death are those that are not directly related to the underlying cause of death but have most likely caused signs of illness and contributed to death.

In our previous necropsy-based study of on-farm dairy cow deaths, mastitis was the most common underlying cause of death (Hagner et al., 2023). When concurrent diseases are present, frequency of inflammatory udder lesions may be underestimated, if only one disease is reported as a cause of death. By examining and reporting all mastitis lesions regardless of other diagnoses or lesions, a more accurate estimation of the frequency of mastitis in on-farm deaths can be achieved. The focus of this paper is on active mammary gland inflammatory lesions in necropsied Finnish dairy cows that had died or been euthanized on-farm. The objectives were to determine (1) what overall role inflammatory udder lesions have in on-farm deaths of dairy cows, (2) what concurrent diseases occur together with mastitis leading to on-farm death, and (3) which factors are associated with detection of mastitis by producers and pathologists.

MATERIALS AND METHODS

Animals and Sample Collection

Our recent necropsy-based study revealed mastitis as the most common underlying cause (85/319) of on-farm dairy cow deaths in Finland (Hagner et al., 2023). Two experienced veterinarians in bovine pathology necropsied 319 dairy cows between September 2020 and August 2021 at an incineration plant (Honkajoki Ltd., Honkajoki,

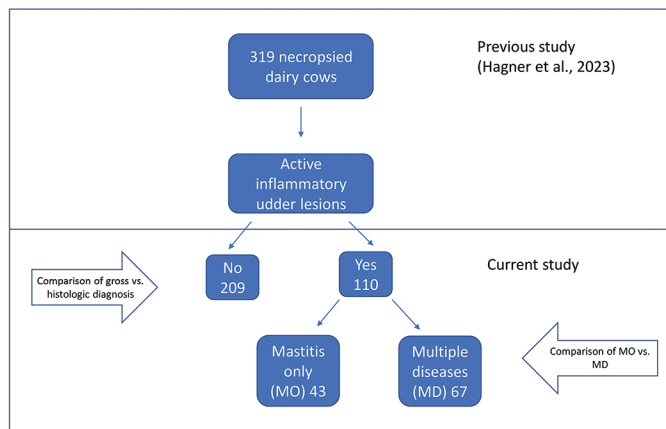


Figure 1. Case inclusion (previous study: Hagner et al., 2023) to determine the number of active inflammatory udder lesions, to compare gross and histopathologic diagnosis, and to compare different mastitis cases.

Finland), which receives cows from all over Finland. In this current paper, we examined all inflammatory udder lesions more thoroughly (Figure 1). Because we did only postmortem sampling, this study did not require approval by an Institutional Animal Care and Use Committee. After necropsy and histopathologic diagnosis, we specifically selected all cows with active inflammatory udder lesions for inclusion in the present study (Figure 1).

At necropsy, the udder was detached, and the teats, udder quarters and supramammary lymph nodes were dissected with multiple cuts. We collected histologic samples from all lesions detected grossly in the mammary gland. In addition, we sampled routinely all udders dorsal to the milk chamber from at least 2 mammary quarters of each necropsied cow. Samples were routinely processed for histopathology. Postmortem mastitis diagnosis was based on inspection and palpation of the udder quarters and dissection of the mammary gland tissue at necropsy (gross diagnosis), and it was further confirmed by histology (histopathologic diagnosis). If diagnosis differed between gross and histopathology, it was coded as changed. Histopathology of the most severely affected quarter determined severity and duration of the inflammatory response at the udder level.

Inflammation was histologically classified as mild if only scattered leukocytes, mostly neutrophils, were present in alveoli and interstitial tissue with mild hyperemia, edema, and neutrophilic leukocytostasis (Figure 2a and 2b). In a moderate inflammation, neutrophils clustered in multiple alveoli in several lobules (Figure 2c and 2d). The interstitial tissue had mild infiltration of neutrophils, along with some other leukocytes (plasma cells, lymphocytes). In a severe inflammation, multiple suppurative to necrotic areas were detected, either in small foci or as large coalescent areas (Figure 2e and 2f). We regarded in-

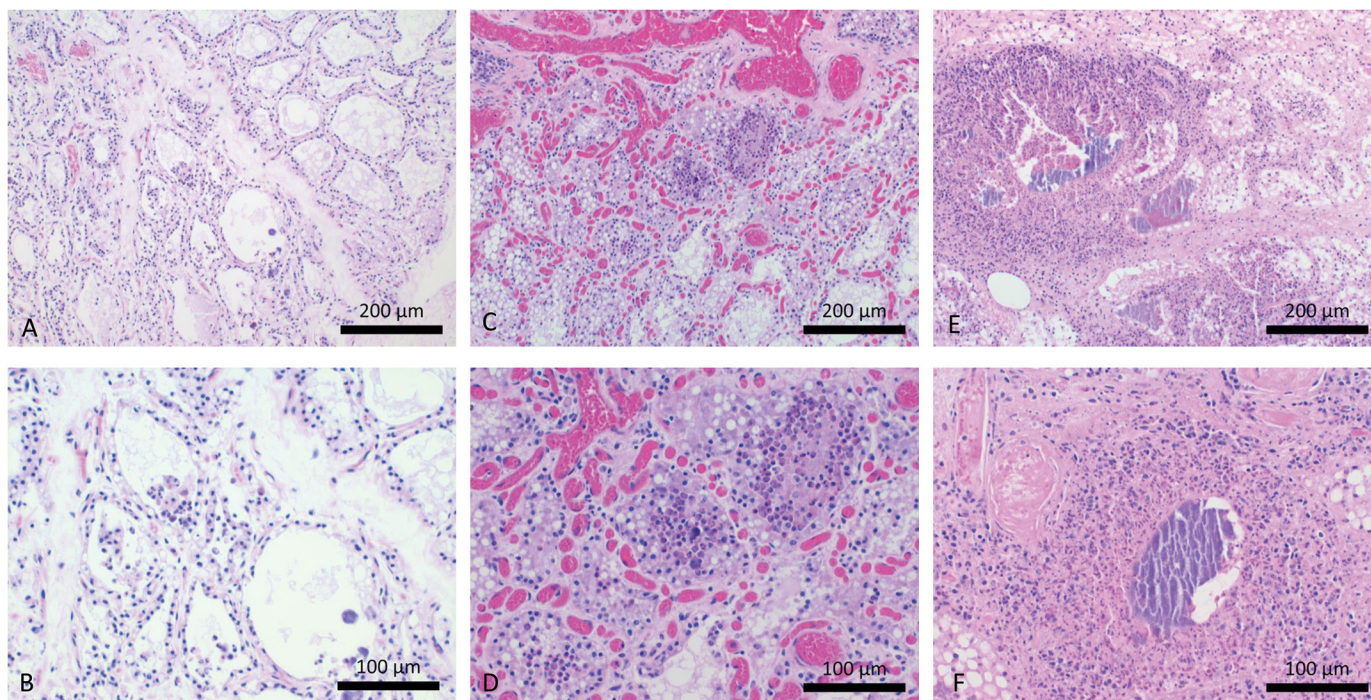


Figure 2. Histopathologic classification of severity of inflammation in affected udders. (A, B) Mild inflammation. Only scattered neutrophils present in occasional alveoli with mild hyperemia and edema. (C, D) Moderate inflammation. Neutrophils clustered in multiple alveoli in several lobules, tissue hyperemic and mildly edematous. (E, F) Severe inflammation. Multiple suppurative to necrotic foci with abundant bacteria and acute thrombosis in blood vessels. All sections stained with hematoxylin and eosin.

inflammation as acute, if leukocyte infiltration was mainly neutrophilic with neither fibrosis, atrophy of glandular parenchyma, nor chronic epithelial changes in alveolar epithelium. In chronic cases, inflammatory cell infiltration was mixed (neutrophils, macrophages, plasma cells, lymphocytes) with chronic changes in alveolar epithelium, and fibrosis, or atrophy of glandular tissue were detected. No cases that showed only inactive lesions in the udder tissue (scattered to small foci of lymphocytes, only fibrotic or atrophic lesions without active inflammation) were included in the study as mastitis cases. We report sensitivity, specificity, and predictive values for gross udder lesions using histopathology as a gold standard. Sensitivity, specificity, and predictive values for gross udder lesions were computed with SPSS statistical package (IBM SPSS Statistics Version 27).

Mastitis was an underlying cause of death when considered as the initial disease starting the causal pathway leading to death. If mastitis resulted from another disease, such as udder trauma or prolonged recumbency, we classified it as an intermediate cause of death. Mastitis was an immediate cause of death when it was the final event just before death. In very acute cases, immediate and underlying diagnoses of death were considered the same. Additionally, mastitis was classified as another significant cause of death, if it influenced

the final outcome but did not fall into any of the aforementioned categories. For example, in cases where mastitis and metritis occurred simultaneously, mastitis was classified as other significant cause of death, if the inflammatory lesion in uterus were more severe than in the udder.

We divided our study cows into 2 groups based on the presence of other diseases detected at necropsy: (1) cases with only mastitis and consequential findings (mastitis only, **MO**) and (2) cases with one or more diseases occurring simultaneously with mastitis (multiple diseases, **MD**). If the cow had active inflammatory udder lesions and lesions that were considered as consequences from mastitis, such as embolic inflammation in other organs or arthritis, it was classified as **MO**. These cows had no other plausible cause for septicemic lesions than mastitis. Furthermore, these cows had no lesions indicative of any other contributing diseases (no other significant causes of death). If the cow had mastitis and at least one simultaneous disease not a direct consequence of mastitis, we classified it as a **MD**. Concurrent mild to moderate abomasal erosion and ulcers were included also as **MO** because the significance of mild to moderate ulcers for cow's well-being is poorly understood (Munch et al., 2019). Any chronic and severe abomasal ulcers or perforations with mastitis we classified as **MD**.

Data Analysis

We compared the occurrence of mastitis (yes, no) in all necropsied dairy cows ($n = 319$) between study periods (January to April, May to August, September to December) using the chi-squared test.

We studied proportions of different breeds, producer-reported signs of mastitis (yes, no), recumbency before death (yes, no), medication within 1 mo (yes, no), duration of illness (1–3 d, over 3 d), type of death (unassisted, euthanized), changed mastitis diagnosis (yes, no), severity of inflammation (mild, moderate, severe), age of cows, and distribution of DIM at death among mastitis-affected cows. We then compared these between MO versus MD using, as appropriate, the chi-squared test, Fisher's exact test, or Mann-Whitney U-test (IBM SPSS Statistics Version 27). We also tested for association between aspiration pneumonia (yes, no) and peroral medication (yes, no) among mastitis-affected cows using the chi-squared test.

To assess characteristics of histopathologic mastitis diagnosis, we used chi-squared test to compare histological severity of inflammation (mild, moderate, severe) versus producer-reported signs of mastitis (yes, no) and number of affected quarters. Chi-squared or Fisher's exact tests, as appropriate, also compared the change in diagnosis (yes, no) versus DIM (0–10 d, 11–150 d, >150 d), study periods (January to April, May to August, September to December), and severity of inflammation (as mild, moderate, or severe).

RESULTS

Study Herds and Cows

In total, we necropsied 319 dairy cows and detected active inflammatory lesions in the mammary gland in 110 of them. Udder lesions were most common in cows in May to August (44%, 47/107), followed by September to December (34%, 36/105), and January to April (25%, 27/107; $P = 0.016$). Cows with mastitis lesions came from 80 herds, with the number of necropsied cows ranging from 1 to 5 per herd. All producers shared farm-level information via an online questionnaire, and we checked responses for obvious errors. Some questionnaires were incompletely filled in, making the number of responses for individual questions vary. Information about average herd size, annual milk yield, calving interval, and number of persons taking care of the herd were missing from 1, 6, 11, and 3 herds, respectively.

The majority of the study herds (95%) were conventional, only a few were organic. Average herd size was 103 cows, annual milk yield 9,957 kg, calving interval 394 d, and number of persons taking care of the herd 2.8.

Most farms (78%) had freestall barns; one-fifth (21%) had a tiestall barn, and only one herd had another housing type. Automatic milking system (AMS) was used in 60% of the herds, 16% of the farms had milking parlors, 23% had tiestall milking, and one farm had multiple milking systems. Cows grazed on pasture during summer in 58% of the herds: both lactating and dry cows were on pasture in 38%, only dry cows in 16%, and only lactating cows in 4% of the herds. When compared with Finnish national dairy herd on average in 2019 the study herds were larger (Finnish national mean in 2019 was 49 cows) and used AMS more often (nationally 37% of herds used AMS; Nokka, 2019). Annual milk yield of the study herds was at the same level as the Finnish national annual mean in 2019 (9,937 kg; Nokka, 2019).

Table 1 includes summary statistics on 110 study cows' DIM, age, breed, parity, duration of illness, signs of mastitis, recumbency, medication, severity of inflammation, type of death, season of death, and change in udder diagnosis based on histopathology. Information was missing for some parameters (n in parentheses): DIM (19), parity (13), duration of signs of illness (10), signs of mastitis (10), and medication during the preceding month (13).

Of the 110 cows with active inflammatory udder lesions, for 12 the pathologists detected no gross lesions in the udder, and the number of affected quarters in those cows could not be determined. For others, one-quarter was affected slightly more commonly (55%) than multiple quarters (45%). Severity of inflammation was not associated with number of affected quarters ($P = 0.854$) but was associated with producer-reported signs of mastitis ($P < 0.001$). Producers reported signs of mastitis during the preceding month in half the cows (49%), and in majority of these cases (94%) inflammation was histologically severe. However, of all the cases where inflammation was histologically regarded as severe, in 28% of them producers had reported no signs of mastitis.

Mastitis Only

Of the total 110 cows with active inflammatory udder lesions, 43 had only mastitis and lesions consequential to it (39%). Mastitis was both the underlying and immediate diagnosis in most of them (95%), and only 2 cows had such severe consequences of mastitis (pulmonary embolism, severe arthritis) that these were established as the immediate cause of death (Table 2). Of these 43 MO cases, 25 cows (58%) were euthanized, 17 (40%) died of sepsis, and one had cardiogenic shock due to pulmonary embolism. The majority of them (79%) had signs of bacterial infection spreading systemically and sometimes in several organs at the same time: most commonly the cows had arthritis (49%), multifocal embolic inflammation in the liver or kidneys or both (26%), and serosal

Table 1. Descriptive statistics for 2 groups of necropsied Finnish dairy cows with active inflammatory udder lesions¹

Item	MO	MD	Total	P-value
DIM at death ² (median, range)	158 (134, 1–396)	99 (34, 0–376)	121 (66, 0–396)	0.006 ³
Age, mean yr (median, range)	5.4 (5.3, 3.3–10.5)	5.8 (5.4, 2.0–10.6)	5.6 (5.3, 2.0–10.6)	0.222 ³
Breed, ⁴ % (n)				0.261 ⁵
Ayrshire	41.9	31.3	35.5 (38)	
Holstein	58.1	68.8	64.5 (69)	
Parity ²				0.517 ⁵
1–2	28.2	22.4	24.7 (24)	
3+	77.8	77.6.3	75.3 (73)	
Duration of signs of illness ²				0.007
0–3 d	81.6	54.8	65.0 (65)	
>3 d	18.4	45.1	35.0 (35)	
Producer-reported signs of mastitis				0.001 ⁵
Yes	69.2	36.1	49.0 (49)	
Recumbent				0.527 ⁵
Yes	37.2	43.3	45 (40.9)	
Medication within 1 mo ²				0.044 ⁵
Yes	50.0	70.5	(61)	
Severity of inflammation				0.010 ⁶
Mild	0.0	9.0	5.5 (6)	
Moderate	11.6	26.9	20.9 (23)	
Severe	88.4	64.2	73.6 (81)	
Type of death				0.750 ⁵
Unassisted	41.9	38.8	44.0 (40)	
Euthanized	58.1	61.2	66.0 (60)	
Season of death				0.511 ⁵
September to December	37.2	28.4	31.8 (35)	
January to April	25.6	23.9	24.5 (27)	
May to August	37.2	47.8	43.6 (48)	
Udder diagnosis changed				0.002 ⁵
Yes	2.3	23.9	115.5 (17)	

¹All values are presented as % (n), unless otherwise noted.

²Information missing: DIM (19), parity (13), duration of signs of illness (10), signs of mastitis (10), medication during previous month (13).

³Mann-Whitney U for distribution of values.

⁴Three were breeds other than Holstein or Ayrshire.

⁵Chi-square test.

⁶Fisher's exact test.

inflammation (peritonitis, pericarditis, pleuritis, 14%; Table 3). Over one-third of these MO cows (37%) also had lesions in the abomasum (mild to moderate, acute or chronic, erosions or ulcers without melena).

Multiple Diseases

More than half of the 110 cows (61%), had, in addition to the active inflammatory lesions in the udder, also other major lesions in multiple organs that were not direct consequences of mastitis (Figure 3). In this category, mastitis was either the immediate (6%), underlying (43%), intermediate (6%), or other important cause of death (27%; Table 2). Mastitis was both the immediate and underlying diagnosis in 18%. In cows with mastitis as the underlying cause of death, the most common immediate cause was aspiration pneumonia (in 59% of them).

The majority of the MD cows (62%) were euthanized; one-fourth (25%) died of sepsis, and 13% of other types

Table 2. Role of mastitis in on-farm deaths among Finnish dairy cows (MO n = 43; MD n = 67; total n = 110)

Mastitis role	MO, n (%)	MD, n (%)	Total, n (%)
Immediate cause ¹		4 (6.0)	4 (3.6)
Underlying and immediate cause ²	41 (95.3)	12 (17.9)	53 (48.2)
Underlying cause ³	2 (4.7)	29 (43.3)	31 (28.2)
Intermediate cause ⁴		4 (6.0)	4 (3.6)
Other significant important cause ⁵		18 (26.9)	18 (16.4)

¹Immediate cause of death is the final outcome just before a cow's death or euthanasia.

²In very acute cases, immediate and underlying causes of death can be the same.

³Underlying cause of death initiates the causal chain reaction leading to death.

⁴Intermediate cause of death is a consequence of an underlying cause.

⁵Other significant or contributing causes of death are those that are not directly related to the underlying cause of death but have most likely caused signs of illness and contributed to death.

Table 3. Organ systems affected in necropsied dairy cows with active inflammatory udder lesions; one cow may have multiple simultaneous lesions (MO n = 43; MD n = 67; total cases n = 110)

Organ system	Lesion	MO, %	MD, %	Total cases, % (n)
Respiratory	Aspiration pneumonia		25.4	15.5 (17)
	Embolic pneumonia		9.0	5.5 (6)
	Bronchopneumonia		9.0	5.5 (6)
	Pleuritis	2.3 ¹	0	0.9 (1)
Reproductive	Metritis		31.3	19.1 (21)
	Rupture or prolapse		4.5	2.7 (3)
	Dystocia		6.0	3.6 (4)
Urinary	Embolic nephritis or acute infarct	7.9	7.4	7.3 (8)
	Pyelonephritis or cystitis		9.0	5.5 (6)
Gastrointestinal	Inflammation or acidosis		10.4	6.3 (7)
	Abomasal erosion or ulcer	37.2 ²	38.8	38.2 (42)
	Torsion or displacement		6.0	3.6 (4)
	Other		4.4	2.7 (3)
Peritoneum	Peritonitis	4.7 ¹	4.4	4.5 (5)
Liver	Embolic hepatitis or abscess	18.6	9.0	12.7 (14)
	Lipidosis	2.3 ³	13.4	9.1 (10)
Circulatory	Endocarditis		6.0	3.6 (4)
	Pericarditis	7.0 ¹	4.4	5.5 (6)
	Other		13.4	8.1 (9)
Skin	Cellulitis, bursitis, abscess	4.7 ⁴	14.9	10.9 (12)
Musculoskeletal	Arthritis	48.8	46.2	47.3 (52)
	Acute trauma		6.0	3.6 (4)
	Other	2.3	3.0	2.7 (3)
Other	Other	2.3	7.5	5.5 (6)

¹Part of systemic serosal inflammatory reaction associated with septicemia.

²Mild to moderate, none with melena.

³Moderate hepatic lipidosis at time of parturition (physiological).

⁴Considered clinically as unimportant.

of shock. Sixty-four percent of these cases had signs of a bacterial infection spreading in the body. Lesions in 3 or 4 organ systems were present in 60% of MD cases, and over one-fourth of them (28%) had lesions in 5 or more

organs. The most frequently affected organ systems were the gastrointestinal tract (60%), musculoskeletal system (55%), respiratory tract (43%), and reproductive tract (42%). The most common lesion in the gastrointestinal tract was abomasal erosions and ulcers (65%), in the musculoskeletal system, arthritis (84%), in the reproductive tract, metritis (78%), and in the lungs, aspiration pneumonia (59%; Table 3).

Among the 67 MD cows, 4 subgroups formed based on the concurrent diseases: (1) mastitis with metritis (27%), (2) mastitis with aspiration pneumonia (25%), (3) mastitis with acute trauma or dystocia (15%), and (4) mastitis with other diseases (33%; Figure 3). Eight of the 17 cows with aspiration pneumonia had only mastitis in addition, and the rest had one or more other simultaneous diseases among which were 3 with metritis. Producers had reported giving oral medication more frequently (77%) to those 17 cows with aspiration pneumonia, than to those 50 cows with no aspiration pneumonia (38%; $P = 0.006$). The subgroup “mastitis and concurrent acute disease/trauma” consisted of acute musculoskeletal traumas, other acute traumas, and calving-related complications. The subgroup of cows with “mastitis and other diseases” most commonly had diseases occurring in the transition period, such as ketosis, hepatic lipidosis, severe rumenitis, or abomasal diseases.

MULTIPLE DISEASES

n=67

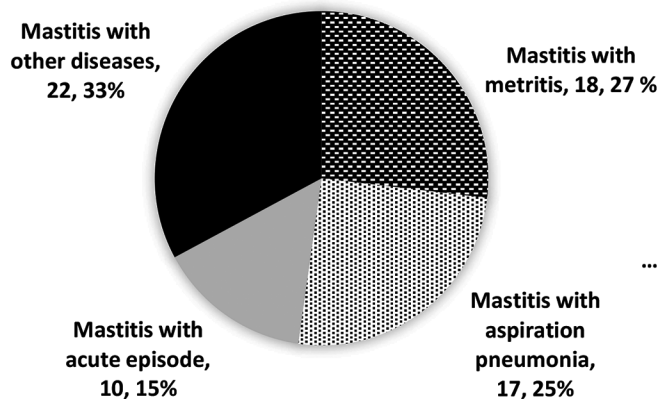


Figure 3. Subgroups of 67 cases with one or more simultaneous diseases occurring simultaneously with mastitis (MD). In the category “mastitis with aspiration pneumonia,” 3 cows also had metritis. The subgroup “mastitis with acute episode” consists of acute musculoskeletal traumas, other acute traumas, and calving-related complications.

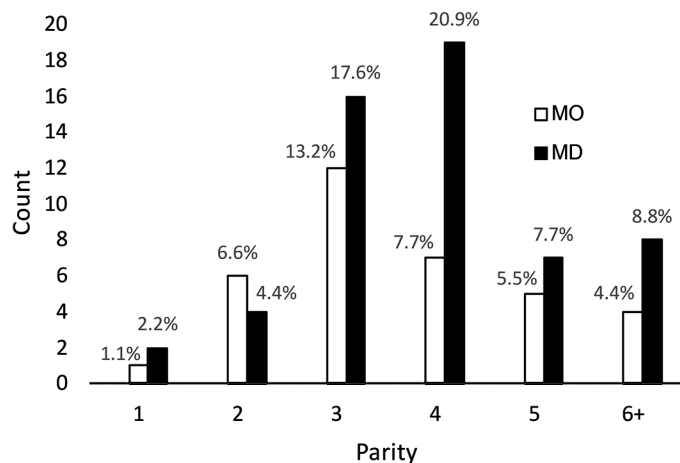


Figure 4. Parity of dairy cows dying on farm with active inflammatory udder lesions in necropsy. Percentages are counted from all cases with active udder lesions (n = 110).

Differences Between MO and MD

Illness duration between MO and MD differed. The MO cows were often acutely ill, and signs of illness lasted over 3 d in only 18% of them. Almost half (45%) of the MD cows, in contrast, had signs of illness lasting over 3 d ($P = 0.007$; Table 1). Producers reported mastitis signs more often (69%) among MO than among MD cows (36%; $P = 0.001$; Table 1). The pathologists also detected mastitis in gross examination more often (98%) in the MO than in MD (76%; $P = 0.002$; Table 1).

Distribution of parities of the cows dying on farm with active inflammatory udder lesions is presented in Figure 4. The MD most often occurred at the beginning of lactation, and the distribution of DIM at death differed between MO and MD (Figure 5; $P = 0.006$). Greater proportion of MO (30%) than MD (12%) occurred after 270 DIM ($P = 0.032$). Of the 17 cases occurring at the end of lactation (DIM >270 d), histopathologic severity of inflammation ranged from moderate (24%) to severe (76%), and all these cases were diagnosed grossly. Producers had reported signs of mastitis in under half (41%) of these late-lactation cases.

Gross Versus Histopathological Diagnosis

The accuracy of the gross mastitis diagnosis was compared with the histopathologically confirmed diagnosis (Table 4). When necropsy revealed no gross lesions in the udder, 91% of those udders were classified as healthy also in the histopathologic examination. Of those cows with the gross mastitis diagnosis, however, only 67% had mastitis in the histopathologic examination. The accuracy of the gross diagnosis varied according to lactation stages: in early lactation (0–10 d) the gross diagnosis

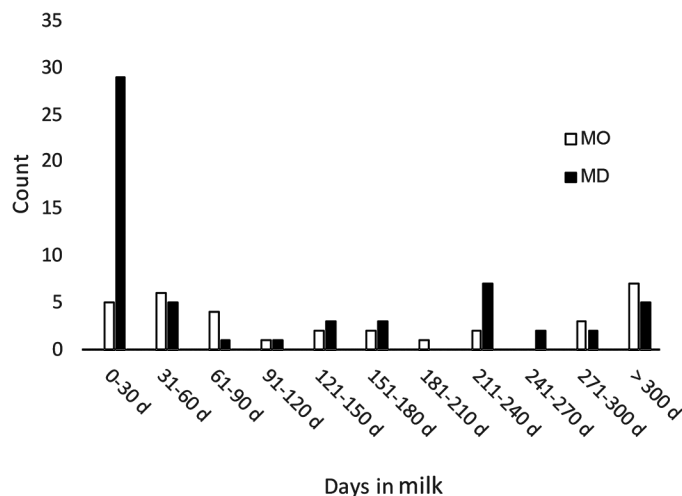


Figure 5. Distribution of MO (n = 43) and MD cases (n = 67) across DIM among 110 cows dying on farm with detectable active inflammatory udder lesions at necropsy.

differed from the histopathologic diagnosis more often (27%) than later during the lactation (d 11–150, 18%). The gross diagnosis was most in line with histopathology after 150 d, because in only 12% of cases, the diagnosis changed ($P = 0.046$). The severity of inflammation affected the accuracy of the gross diagnosis: in only 7% of severe cases the gross diagnosis changed after histopathologic evaluation, followed by 35% changing in moderate, and 50% changing in mild mastitis lesions ($P < 0.001$). The accuracy of the gross mastitis diagnosis did not differ between study periods: 76% of the diagnoses made in May to August, 80% in September to December, and 84% in January to April did not change ($P = 0.273$).

DISCUSSION

In current study of on-farm mortality, one-third (110/319) of dairy cows had active inflammatory udder lesions. Mastitis occurred either as the only disease leading to the death (39%) or was interacting with other simultaneous diseases (61%). No previous studies have

Table 4. Accuracy of gross mastitis diagnosis versus final histopathologically confirmed mastitis diagnosis (+, positive; –, negative)¹

Item	Histopathology +, % (n)	Histopathology –, % (n)	Total, % (n)
Gross +, n (%)	29.5 (94)	41.8 (46)	43.9 (140)
Gross –, n (%)	5.0 (16)	51.1 (163)	56.1 (179)
Total	34.5 (100)	65.5 (209)	100.0 (319)

¹Sensitivity = $94/110 = 0.855$ (95% confidence level 0.775–0.915). Specificity = $163/209 = 0.78$ (95% confidence level 0.718–0.834). Positive predictive value = $94/140 = 0.671$. Negative predictive value = $163/179 = 0.911$.

reported necropsy-confirmed occurrence and significance of mastitis in on-farm deaths of dairy cows.

Occurrence of Mastitis

Mastitis is among the most common causes of dairy cow culling (Rajala-Schultz and Gröhn, 1999; Rilanto et al., 2020; Thomsen, 2023). Many studies have demonstrated an association between parity and mastitis (Persson Waller et al., 2009; Heikkilä et al., 2012; Fukushima et al., 2020). Our results indicate this also with on-farm deaths, as most cows with active inflammatory udder lesions were at their third lactation or beyond. Older study cows—third or later lactation—exhibited one or more simultaneous diseases along with mastitis more often than younger ones. This may indicate that in the early stages of a cow's productive life, the role of mastitis in on-farm deaths is minor but later increases, and at the same time, multiple diseases occur together more commonly.

Clinical mastitis is most common at the beginning of lactation (Thomsen et al., 2004; Olde Riekerink et al., 2007; Rilanto et al., 2020). In our study, the majority of cases with MD occurred shortly after calving. In contrast, MO cases occurred quite evenly throughout the lactation period, with only a minor peak at the beginning and at the end of the lactation period. Producers reported mastitis signs in less than half of the cases occurring either in late lactation or in the dry period (DIM >270 d), even though histopathologic inflammatory lesions were usually severe. The udder is susceptible to new IMI during the early and late dry period (Bradley and Green, 2000), and these infections are often detected around or after calving, manifesting themselves as severe clinical cases (Fredebeul-Krein et al., 2022).

Of the 110 cows with inflammatory udder lesions, 39% of cases were classified as MO, and 61% as MD. This suggests that in 61% of cows preventing premature death requires consideration of multiple simultaneous diseases. Our results also indicate that in any cow with signs of disease, it is important to detect possible concurrent mastitis. Particularly during the dry period, when udders are not handled daily, and in recumbent cows, mastitis signs can be easily missed. Dry cows have higher probability to die unassisted and for unknown reasons than lactating cows (Fusi et al., 2017). We suggest that the examination of the udder of dry cows and all sick cows could serve as an inexpensive tool to detect and subsequently treat mastitis as early as possible to improve prognosis. By decreasing mastitis occurrence in the herd, the health and animal welfare would improve on dairy farms. On-farm deaths are regarded as a potential indicator of decreased welfare in dairy cows (Thomsen and Houe, 2018), making any measures that reduce mortality valuable tools in ensuring animal welfare.

Lesions and Diseases Occurring Concurrently with Mastitis

We observed that arthritis was a common lesion occurring in Finnish dairy cows with inflammatory udder lesions. Arthritis was most often interpreted as a consequence of mastitis, because joint lesions were milder and more acute than were mastitis lesions. In addition, for arthritis in adult cows, hematogenous infection is reportedly the most common route (Nuss, 2000). Only 4 MD cows had arthritis that was more severe and chronic than their mastitis, and 3 of these cows also had infections in other organs, making the role of mastitis as the bacteremia source unclear. A veterinarian's clinical examination may underestimate the severity of bovine septic arthritis (Nuss, 2000), and probably this is true for producer-reported signs of lameness as well. In cows with mastitis, arthritis signs were likely mild and transient, because the producers in our study had reported signs of lameness rarely.

In our study, embolic lesions were common, with indications of spreading infection in the body present in 70% of cows. Embolic lesions were most frequent in the liver, then in the kidneys and the lungs. Some cows had embolism in several organs concurrently. Although MD cows could have multiple causes for embolism, we found no significant difference in the proportion of cows with embolic lesions between MO and MD. Endocarditis resulting from embolism was rare and evident only in MD. Embolic lesions are indicative of previous bacteremia; in earlier studies, the proportion of cows with bacteremia during severe mastitis has ranged from 1% to 42% (Wenz et al., 2001; Brennecke et al., 2021; Krebs et al., 2023).

Aspiration pneumonia was one of the most common findings in MD cows. These cows had more commonly received oral medication than cows without aspiration pneumonia. Half of the cows with aspiration pneumonia had no additional significant lesions apart from mastitis. Peroral medication is an important risk factor for aspiration pneumonia; however, some cows with aspiration pneumonia had no anamnestic information about peroral medication. Other predisposing factors, such as hypocalcemia or recumbency, may have played a role in causing aspiration pneumonia, or the peroral medication was simply not reported. In one necropsy-based study, half the dairy cows had lung lesions, but the report omitted mentioning any causes for them (McConnel et al., 2010). In that study peroral medication was very common. However, it is not clear from their results if the cows with lung lesions had received peroral medication (McConnel et al., 2010).

One-third of the MD cows had metritis and mastitis simultaneously and had recently calved. The postpartum period is a risk period for both metritis (Risco et al.,

2007; Sheldon, 2019) and mastitis (Valde et al., 2004; Persson Waller et al., 2009; Aleri et al., 2021). Only a few studies report on simultaneous occurrence of diseases in the transition period (Curtis et al., 1985; Correa et al., 1993), and only one has reported an association between severe clinical mastitis and metritis (Fredebeul-Krein et al., 2022). Both mastitis and metritis can have the same causal pathogens, for example *Escherichia coli* or *Trueperella pyogenes* (Hazlett et al., 1984; Risco et al., 2007). During the puerperal period an important risk factor for *E. coli* infections may be weakened immunity (Burvenich et al., 2007), thus either a direct or indirect association may exist between these diseases. One earlier necropsy-based study has reported cows with fatal *E. coli* mastitis also having concurrent endometritis (Hazlett et al., 1984).

Necropsies and Histopathology

Necropsy-based studies on dairy cows are sparse, and those reporting lesions especially in the udder even fewer. In a decade-old study of 3 high-yielding herds in Colorado, one-fourth of the necropsied dairy cows had udder lesions (McConnel et al., 2010). In that study, a veterinarian had diagnosed mastitis clinically before necropsy. In our study, the producers provided histories for the cows; however, in about half the cows with mastitis lesions, the producers reported no signs of mastitis during the last month of the cow's life. In over one-fourth of these cases (28%), however, mastitis was regarded postmortally as severe. Within MO cows, the producers reported mastitis signs more often than with multiple diseases. Simultaneous signs of various diseases can mask each other, making it harder for producers to detect mastitis, or producers may not regard mastitis signs as sufficiently important to report. In addition, in recumbent cows, it can be difficult to examine the udder. It is important, however, to keep in mind that severe mastitis can also result in recumbency (Braun et al., 2021). In our study, 37% of MO cases had been recumbent, according to producer reporting.

Although the histology of bovine udder and mastitis has been under study since the 1860s (Fürstenberg, 1868; Helmboldt et al., 1953; Yamagiwa et al., 1957), no common standards exist for histologic classification of mastitis severity, nor for its duration (acute or chronic). Nor does any standardized nomenclature exist. Earlier studies related to udder histology of naturally occurring mastitis cases have mainly used slaughtered dairy cows (Benites et al., 2002; Hussain et al., 2012; Bianchi et al., 2019; Leitner et al., 2020). Material from a slaughterhouse and from an incineration plant differ, and the severity and type of the udder inflammatory lesions can also differ markedly. Studies based on mastitis histopathology have

not compared the number and type of inflammatory cells in the udders with the signs of clinical mastitis, nor with the existence of subclinical mastitis (Bianchi et al., 2019; Leitner et al., 2020).

We compared producer-reported signs of mastitis with the severity of inflammatory lesions, and in some cases classified as mild, a producer had detected signs of mastitis during the preceding month. In other mild cases, the history failed to mention mastitis signs. In future studies, comprehensive knowledge of a cow's entire mastitis history, SCC, bacterial culture of milk and of tissue from all quarters, along with clinical signs, are essential to establish standards for histopathologic classification of mastitis. This will enable comparison of each histopathological diagnosis to the clinical status of that cow (healthy, subclinical, clinical mastitis) leading to improved understanding between clinicians and pathologists regarding the relevance of inflammatory udder lesions. Veterinary clinicians and producers often consider clinical mastitis to be an acute process. Still, from the pathological point of view, in many clinical cases, fibrosis, atrophy, or regeneration are present, indicating that inflammation is already chronic, and mastitis may have existed subclinically for a long time. This may cause confusion between clinical and pathological diagnoses regarding inflammation duration and the role of mastitis in a cow's death.

Our previous study (Hagner et al., 2023) pointed out that histopathology can give marked additional information or change the underlying diagnosis in 18% of necropsies. From human pathology, it is known that the usefulness of histopathology varies between organs (Parai and Milroy, 2018). Some studies have compared gross and histopathologic diagnosis of pulmonary lesions in bovine necropsies and observed that the accuracy of gross diagnosis differs between pneumonia types. Except for bronchopneumonia, gross diagnosis should be considered only as a preliminary diagnosis before histopathology is conducted (Haydock et al., 2023; Schmidt et al., 2023).

Our current paper highlights the fact that histologic samples are valuable in detecting udder inflammatory lesions, especially in mild and moderate mastitis lesions occurring in the beginning of lactation in cows with multiple diseases. Our gross examination of the udder proved to be a moderately sensitive tool for diagnosing mastitis in necropsied dairy cows, and false-negative results were uncommon, when histopathologic examination was the gold standard. Lactation stage affected the accuracy of macroscopic diagnosis; in the beginning of lactation, udder lesions were more challenging to interpret grossly due to the hyperemia, edema, and the appearance of colostrum. This implies that for a pathologist to interpret udder lesions accurately, a history concerning

lactation stage is crucial. Furthermore, the accuracy of mastitis diagnosis between study periods (season when necropsies were performed) did not differ; thus, seasonal weather conditions, such as freezing or high temperature, did not affect.

This study had some limitations. Because the study material was collected at an incineration plant, carcasses and tissues were not sufficiently fresh for any reliable microbiologic testing. As a result, no bacteriological cultures from milk or mammary gland tissue could not be obtained. In the future, it would be interesting to study which bacteria are most commonly isolated from milk and udder quarters of cows dying on-farm due to mastitis, but the sampling should occur ante mortem. For those cows for which the producer had not noticed or reported any signs of mastitis, we cannot be sure how the postmortem mastitis diagnosis related to the cow's clinical status. Unfortunately, we had no information on the study cows' somatic cell counts or earlier mastitis history. However, mild and moderate cases represented only a minority of our cases.

CONCLUSIONS

This study was conducted on Finnish dairy cows that died or were euthanized on farm and had active inflammatory udder lesions (mastitis) in postmortem examination. Of all the cows with pathologic lesions in the mammary gland, 39% had only mastitis and consequential findings leading to their death (MO), whereas 61% of the dead cows had in addition to mastitis concurrent contributing diseases (MD). Mastitis detection seems to be influenced by other concurrent diseases, stage of lactation, and severity of inflammation. Cases with MD occurred mainly at the beginning of lactation, whereas MO cases occurred quite evenly throughout the production cycle. Our results indicate that even with clinical signs of other diseases, the udder should be considered a potential cause of illness, and it should be examined, especially in dry and transitional cows. The most common lesions occurring together with mastitis were abomasal erosions or ulcers, arthritis, metritis, and aspiration pneumonia. Histopathology for diagnosing udder lesions was most useful at the beginning of lactation in cows with multiple concurrent diseases.

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Nonstandard abbreviations used: AMS = automatic milking system; MD = cases with one or more diseases occurring simultaneously with mastitis; MO = cases with mastitis and consequential findings.

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