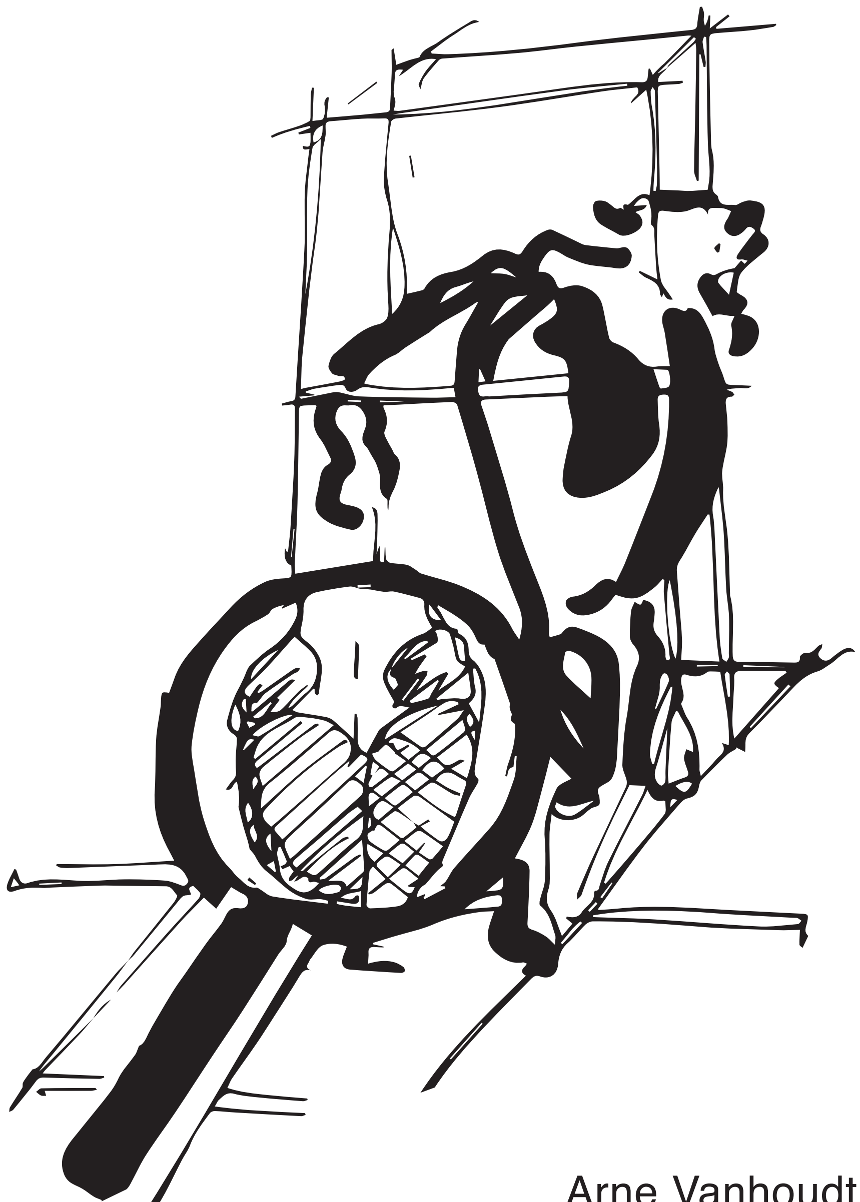
Diagnosis, treatment, and control of bovine digital dermatitis in dairy cattle



Arne Vanhoudt

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Diagnosis, treatment, and control of bovine digital dermatitis in dairy cattle

De diagnose, behandeling en beheersing
van digitale dermatitis bij melkvee
(met een samenvatting in het Nederlands)

Proefschrift

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Contents

Summary

BACKGROUND

Lesions of digital dermatitis are the leading cause of infectious lameness in dairy cattle worldwide, thereby negatively affecting animal welfare and farm economics through production loss, decreased reproductive performance, treatment costs, and increased risk of culling. In Europe, about 85% of the herds are reported infected and within-herd digital dermatitis prevalence ranges between 3 and 83%.

Current consensus is that digital dermatitis is a polymicrobial and multifactorial disease. Poor foot hygiene is an important risk factor for digital dermatitis as it contributes to skin maceration and reduced access to air, which are considered essential pre-conditions for inducing digital dermatitis lesions. *Treponema* spp. have a fundamental role in lesion development and are identified in all lesions of digital dermatitis. Hence all lesion stages of digital dermatitis are considered infectious.

The majority of lesions are seen in lactating dairy cattle, but in infected herds, usually a proportion of the dry cows and youngstock are also affected. Lesions of digital dermatitis typically affect the plantar or palmar aspect of the pastern region of the foot on the border of skin and horn, with hind feet affected most. Various digital dermatitis grading and scoring systems exist, with the simplest and most reliable system involving recording the presence or absence of a digital dermatitis lesion. A popular and widely used scoring system is the M-score, which identifies six epidemiologically significant lesion categories. The 'M' stands for "Mortellaro" and the number for disease stage. Normal unaffected skin is classified as M0. The M1-stage is considered the early stage of digital dermatitis. Lesions of the M1-stage are described as a circumscribed granulomatous epithelial erosion, <2 cm in diameter. An M2-stage lesion is characterized by ulceration >2 cm in diameter, redness, a pungent odor, swelling, and is often painful causing lameness. The M3-stage is characterized by a dry dark brown to black crust which is not painful. The M3-stage lesions typically can be

seen within a few days after topical treatment of the ulcerative lesions. The majority of lesions eventually transition to the M4-stage. The M4-stage is the chronic stage of digital dermatitis and presents itself as a brown to black rubbery hyperkeratotic lesion. Within these M4-stage lesions, sometimes small ulcerative areas, reflecting M1-stage lesions, develop. This resulted in the addition of the M4.1-stage lesion to the M-score. The ulcerative stages (M1, M2, and M4.1) are often grouped as active lesions and the M3- and M4-stages as chronic lesions. It is important to note that the M-scores do not represent a linear progression or severity scale, but are a way of capturing epidemiologically significant lesion stages.

A remarkable aspect of digital dermatitis lesions is that after initial lesion improvement following topical treatment, a substantial amount of lesions demonstrate recrudescence to more severe, ulcerative lesion stages.

All lesions of digital dermatitis can be painful with the degree of perceived pain varying between lesions stages and cows. This discomfort, especially when resulting in lameness, is likely to alter the behaviour of infected animals and is the underlying mechanism associated with decreased reproductive performance and production losses.

Management of digital dermatitis in dairy herds is achieved at two levels. First, there is a need to control infection pressure within the herd. The observation that foot lesions in cattle are the main source and reservoir of infection suggests that control measures should focus primarily on treatment and biocontainment of animals with non-regressing lesions, and also the protection of uninfected animals with good foot hygiene, cleaning, and disinfection protocols. This is typically done using biocide containing footbaths together with other management practices. Second, there is the need to treat painful lesions to warrant animal welfare and reduce production losses. Many of the aspects of current digital dermatitis control are labor-intensive, expensive, detrimental for the environment, pose a health-risk for the farm-worker, or a combination of these. With the exception of one case report, these intensive control programs, however do not eradicate digital dermatitis from herds, but at best result in achieving a manageable state of the disease, with the best dairy herds having less than 10% of cows affected and less than 1% of cows having an active lesion.

Chapter 2 of this thesis provides an overview of the status quo on management of digital dermatitis on dairy herds, with the exception of prevention. Based on literature and expert opinion, the identification of animals eligible for treatment, treatment strategies, and herd level control through footbaths is reviewed. The next chapters in this thesis describe four applied field studies that were carried out to enhance the scientific evidence related to the management of digital dermatitis: two studies on diagnosis, one on the treatment of active lesions, and one on herd level control.

DIAGNOSIS OF DIGITAL DERMATITIS

The identification and classification of digital dermatitis lesions is not straightforward due to their anatomical location and the various aspects in which lesions present themselves. For any classification system to be valid, its users need to be able to assign the same score to the same lesion, each time the lesion is scored. This is often expressed as intra- and interobserver agreement and determines the validity of published research using the classification system. In Chapter 3 we assessed the interobserver agreement of the M-score by unstandardized, independent, experienced scorers, using single, digital color photographs of standing dairy cattle hind feet. We demonstrated that experienced scorers are well able to differentiate between photographs of feet affected by digital dermatitis and photographs of feet unaffected by digital dermatitis. On the other hand, they were less able to identify specific lesion stages, including the M2- and M4-stage which are considered important stages as related to clinical impact and infection reservoir, respectively.

To date, inspection of the feet in a foot trimming chute is considered best practice for the diagnosis of digital dermatitis. This practice is labor-intensive and despite good cattle handling, cows often experience a degree of stress during the procedure. Alternatively, screening for digital dermatitis in the milking parlor, at the feed rail, or during pen walks has been validated with varying but often mediocre test characteristics. To enable automated detection, efforts were made using infrared thermography or computer vision and machine learning. In Chapter 4 we tested the association between skin temperature measured by infrared thermography and the presence of M2 lesions under farm conditions, with the ultimate goal of automated lesion detection. We concluded that infrared thermography is unlikely to be useable for automated identification of feet affected by digital dermatitis due to the poor associations between maximum temperature of the plantar pastern region and the presence of M2 lesions or digital dermatitis lesions in general.

TOPICAL TREATMENT OF DIGITAL DERMATITIS LESIONS

A plethora of products for topical treatment of digital dermatitis lesions were studied, with most having an antimicrobial component. Whether or not these products should be applied under a bandage is still the topic of much debate, with current evidence in favor of bandaging. The majority of these topical treatments mitigate the pain associated with digital dermatitis lesions, but fail to achieve cure, i.e. return to unaffected skin, in a substantial number of lesions.

In Chapter 5 we investigated the effect of two non-antibiotic gels [a copper and zinc chelates gel (coppergel) and an enzyme alginogel] under bandage on hind feet with active digital dermatitis lesions in dairy cattle. Treatment effect was assessed using the M-score and wound healing progress criteria. The coppergel outperformed the alginogel in M-score improvement, resulting in a manageable state of disease, with the majority of lesions remaining in the chronic state. In contrast, the alginogel achieved improved wound healing progress compared with the coppergel. However, none of the products used in our study achieved high cure rates (return to the M0-stage) for active digital dermatitis lesions.

CONTROL OF DIGITAL DERMATITIS

Many studies identified risk factors and control measures associated with digital dermatitis variation between herds. Particularly factors related to foot health and housing management can potentially be adapted by a farmer to facilitate digital dermatitis control. In Chapter 6 we utilized an available checklist based on reported risk factors to carry out farm specific risk assessments with the aim to raise awareness of the digital dermatitis prevalence and to provide the farmer and the veterinarian with specific control options. We illustrated that a standalone identification of risk factors for digital dermatitis together with associated advice to control these risk factors is insufficient to decrease the prevalence of digital dermatitis in dairy herds.

CONCLUSIONS

Managing digital dermatitis in dairy herds relies on the early detection and prompt effective treatment of lesions, combined with controlling transmission of the disease within the herd. To date, the detection of digital dermatitis remains time-consuming, especially when done frequently to allow early detection of active lesions. Techniques using computer vision and artificial intelligence seem to have the best potential to automate digital dermatitis detection. The treatment of digital dermatitis currently focuses on topical treatment of active lesions to deal with their negative effect on production and animal welfare. Yet, most treatment protocols result in the transition of lesions to the chronic stage and few achieve high levels of cure to unaffected skin, including bacteriological cure. With several non-antibiotic products resulting in similar or better treatment outcomes, there does not seem to be a role for topical antibiotics in the treatment of digital dermatitis. Although the evidence is still weak, the use of bandages appears to result in better cure rates. Controlling digital dermatitis at the herd level includes reducing the number of infected animals through lowering the prevalence of animals with lesions, avoiding disease transmission by minimizing the contact of cows' feet with slurry, and decreasing the susceptibility of the herd for digital dermatitis through genetic selection. Bringing all these factors together not only requires farm advisors to be knowledgeable, but they will also need to be good communicators and strong motivators.

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Samenvatting

ACHTERGROND

Digitale dermatitis wordt in Nederland in de volksmond ook wel "Mortellaro" genoemd en is wereldwijd de belangrijkste infectieuze klauwaandoening bij melkvee. Digitale dermatitis heeft een negatief effect op het dierenwelzijn en de economische rendabiliteit van melkveebedrijven door verminderde productie, slechtere vruchtbaarheid, behandelkosten en een verhoogde kans op vroegtijdige afvoer van aangetaste runderen. Digitale dermatitis komt voor op het merendeel van de Europese melkveebedrijven en het percentage besmette koeien binnen een bedrijf kan oplopen tot wel 85%.

Digitale dermatitis is een multifactoriële aandoening met een multimicrobiële etiologie. Een slechte hygiëne van de ondervoet is één van de belangrijkste risicofactoren voor digitale dermatitis. Slechte hygiëne van de ondervoet door aangekoekte mest draagt bij aan maceratie van de huid en het creëren van een anaeroob milieu. Deze twee factoren blijken in onderzoeken essentieel voor de inductie van letsels van digitale dermatitis. Daarnaast is er een sleutelrol weggelegd voor *Treponema* spp. in het ontstaan van de letsels. In alle letsels van digital dermatitis worden *Treponema* spp. gevonden en volgens de huidige inzichten worden dan ook alle letsels als infectieus beschouwd.

De letsels van digitale dermatitis komen het meest voor aan de achterzijde van de ondervoet van achterpoten van melkgevende runderen. Op besmette bedrijven worden ook regelmatig letsels van digitale dermatitis gevonden bij een deel van de droge koeien en het jongvee. Het klassieke letsel van digitale dermatitis is een ulceratieve huidontsteking aan de achterzijde van de poot ter hoogte van de overgang tussen de balhoorn en huid. Het meeste gebruikte classificatiesysteem voor de letsels van digitale dermatitis is de M-score. De M-score bestaat uit zes belangrijke stadia binnen de epidemiologie van digitale dermatitis. Hierin staat de 'M' voor "Mortellaro" en het nummer voor het stadium van het letsel. Het M0-stadium wordt gebruikt voor onaangetaste huid; M1 is een klein

(<2 cm) oppervlakkig ulceratief letsel; M2 is het klassieke ulceratieve letsel met een doormeter >2 cm en is doorgaans pijnlijk bij aanraking; M3 is een letsel bedekt door een korst en wordt typisch enkele dagen na topicale behandeling gezien; M4 is het chronische stadium en is gekenmerkt door een bruin-zwart hyperkeratotisch letsel; M4.1 is een M4 letsel met daarin een M1 letsel. Binnen de M-score worden de ulceratieve letsels (M1, M2 en M4.1) gegroepeerd als actieve letsels en het M3- en M4-stadium als chronische letsels. Ondanks de numerieke opeenvolging van de stadia in de M-score, zien we in de praktijk een verscheidenheid aan transities tussen de verschillende stadia. Het is belangrijk op te merken dat de M-score geen rangorde is van klinische ernst of epidemiologisch belang van het letsel.

Het resultaat van de meeste huidige topicale behandelingen van de actieve letsels van digitale dermatitis is een transitie naar het chronische M4-stadium in plaats van genezing naar onaangetaste huid (M0). Opmerkelijk hierbij is dat een substantieel deel van deze chronische letsels na verloop van tijd weer hervalt in meer ernstige, ulceratieve letsels.

Alle letsels van digitale dermatitis kunnen pijnlijk zijn, waarbij er een variatie in pijnlijkheid gezien wordt afhankelijk van M-stadium en koe. Actieve letsels zijn pijnlijker dan chronische, met het M2-stadium als meest pijnlijk. Met name wanneer er sprake is van kreupelheid, resulteert deze pijn in gedragsveranderingen bij de koe, die ten grondslag liggen aan de negatieve effecten op melkproductie, vruchtbaarheid en verhoogde kans op vroegtijdige afvoer.

Het management van digitale dermatitis op bedrijfsniveau bestaat uit twee aspecten. Enerzijds het verminderen van de infectiedruk op het bedrijf. De vaststelling dat poten met letsels de grootste bijdrage leveren aan het infectiereservoir, suggereert dat controlemaatregelen best focussen op de behandeling en isolatie van dieren met letsels en het beschermen van niet-geïnfecteerde dieren door middel van goede hygiëne en desinfectie. Dit laatste wordt gedaan door het gebruik van klauwbaden met een biocide en maatregelen in het bedrijfsmanagement gericht op het optimaliseren van de hygiëne. Anderzijds dienen de pijnlijke letsels individueel behandeld te worden. Dit bevordert het dierenwelzijn en beperkt productieverliezen. Veel van bovengenoemde maatregelen zijn arbeidsintensief, hebben een negatief effect op het milieu, vormen een risico voor de gezondheid van de veehouder of een combinatie hiervan. Ondanks volgehouden inspanningen resulteert dit doorgaans niet in eradicatie, maar in een beheersbaar niveau van digitale dermatitis op een melkveebedrijf. De beste bedrijven slagen erin om minder dan 10% van de dieren met letsels van digitale dermatitis te hebben en minder dan 1% van de dieren met actieve letsels.

Hoofdstuk 2 van dit proefschrift geeft een overzicht van de huidige inzichten in het management van digitale dermatitis op melkveebedrijven. Op basis van persoonlijke ervaringen en wetenschappelijke literatuur worden de identificatie van dieren voor behandeling, behandelprotocollen en de beheersing op koppelniveau door middel van klauwbaden besproken. In de volgende hoofdstukken worden vier veldstudies over digitale dermatitis beschreven: twee studies over de diagnostiek van letsels, één over de behandeling van actieve letsels en één over beheersing op koppelniveau.

DIAGNOSTIEK VAN DIGITALE DERMATITIS

Omwille van hun anatomische locatie op de ondervoet en de verscheidenheid aan vormen waarop de letsels van digitale dermatitis zich manifesteren, is de identificatie en classificatie van deze letsel niet vanzelfsprekend. Voor de betrouwbaarheid van een classificatiesysteem, is het belangrijk dat verschillende gebruikers steeds eenzelfde score geven aan hetzelfde letsel (interobserver agreement), ook bij herhaaldelijk scoren van het letsel door dezelfde gebruiker (intraobserver agreement). In hoofdstuk 3 hebben we aan de hand van digitale kleurenfoto's van achterpoten van staande melkkoeien de interobserver agreement bepaald voor de M-score door onafhankelijke, ervaren scorers. Hieruit blijkt dat ervaren scorers over het algemeen goed het onderscheid kunnen maken tussen foto's van poten met digitale dermatitis en foto's van poten zonder digitale dermatitis. Deze scorers waren daarentegen minder goed in het differentiëren tussen de verschillende stadia van de M-score, waaronder het M2- en M4-stadium. Deze twee stadia hebben een belangrijke rol binnen de problematiek van digitale dermatitis. Het M2-stadium omwille van het nadelige effect op dierenwelzijn en productie en het M4-stadium omwille van het belang als infectiereservoir in de epidemiologie.

Om een zo nauwkeurig mogelijke diagnose van digitale dermatitis te stellen is een inspectie van de poot en tussenklauwspleet in de bekapbox nodig. Dit is echter tijdrovend en arbeidsintensief, zeker wanneer het hele koppel geïnspecteerd moet worden. Bovendien wordt de procedure in min of meerdere mate als stressvol ervaren door de koeien. Alternatieve methoden om een koppel koeien te screenen op de aanwezigheid van letsels van digitale dermatitis zijn het scoren in de melkput, aan het voerhek of tijdens een rondgang in de stal. Deze alternatieven hebben echter vaak een beperkte sensitiviteit en specificiteit. Om de detectie van koeien met digitale dermatitis te automatiseren zijn infrarood thermografie en computer visie met artificiële intelligentie onderzocht. In hoofdstuk 4 hebben we onder bedrijfsomstandigheden onderzocht of de huidtemperatuur van de typische anatomische locatie van digitale dermatitis, gemeten met infrarood thermografie, geassocieerd is met de aanwezigheid van M2 letsels. Het uiteindelijk doel hiervan was de automatische detectie van poten met M2 letsels van digitale dermatitis. Hierbij vonden we een zwakke associatie tussen de maximale infrarood temperatuur van de poothuid en de aanwezigheid van M2 letsels of letsels van digitale dermatitis in het algemeen. Het instellen van een grenswaarde voor de maximale infrarood temperatuur waarboven een M2 letsel aanwezig zou zijn, resulteerde echter in een drastische vermindering van de betrouwbaarheid van deze associatie. Hierdoor lijkt het onwaarschijnlijk dat infrarood thermografie een geschikte technologie is voor de automatische detectie van poten met digitale dermatitis.

TOPICALE BEHANDELING VAN LETSELS VAN DIGITALE DERMATITIS

Voor de topicale behandeling van digitale dermatitis zijn er verscheidene middelen beschikbaar en onderzocht. De meeste van deze middelen hebben een antimicrobiële component. Over het al dan niet gebruiken van een verband in de behandeling van digitale dermatitis zijn de meningen verdeeld. Met name vanuit een angst voor verbandletsels als gevolg van verbanden die te nat worden of te laat verwijderd worden. In de schaarse studies die het effect van verbanden in de behandeling van digitale dermatitis onderzocht hebben, worden de beste resultaten behaald met behandelprotocollen met verband. Echter, met het merendeel van de topicale behandelingen van actieve letsels van digitale dermatitis wordt wel een transitie naar een minder tot niet pijnlijk chronisch stadium bewerkstelligd, maar zelden leidt dit tot een genezing naar onaangetaste huid. In hoofdstuk 5 onderzochten we het effect van twee antibioticumvrije gels [een koper en zink chelaten gel (kopergel) en een enzyme alginaatgel] onder verband op actieve letsels van digitale dermatitis. Het effect van deze behandeling werd na 10 dagen beoordeeld aan de hand van de M-score en criteria met betrekking tot wondgenezing. De kopergel behaalde betere resultaten dan de aglinaatgel voor wat betreft de M-score, met veelal een transitie naar chronische letsels (M3 en M4). Daarentegen resulteerde een behandeling met de alginaatgel in een betere wondgenezing van de letsels in vergelijking met de kopergel. Desalniettemin genazen maar een zeer klein deel van de letsels naar onaangetaste huid (M0) ongeacht de gel waarmee ze behandeld werden.

BEHEERSING VAN DIGITALE DERMATITIS OP KOPPELNIVEAU

Verscheidene studies hebben de risicofactoren en beheersmaatregelen voor digitale dermatitis in kaart gebracht. Met name factoren geassocieerd met klauwgezondheid en huisvesting kunnen door veehouders gebruikt worden om digitale dermatitis te beheersen bij hun melkvee. In hoofdstuk 6 is er door middel van een enquête op basis van de wetenschappelijke literatuur een risicoanalyse uitgevoerd op melkveebedrijven samen met een prevalentiebepaling van digitale dermatitis door middel van M-scoren in de melkput. Het doel hiervan was om bewustwording te creëren bij de veehouder en de begeleidende dierenarts, gericht op verbetering van het management van digitale dermatitis op deze bedrijven. Twee jaar na het eerste bedrijfsbezoek werden de risicoanalyse en prevalentiebepaling herhaald. De resultaten van dit onderzoek laten zien dat een éénmalige identificatie van de belangrijkste risicofactoren voor digitale dermatitis onvoldoende is om de prevalentie van digitale dermatitis op melkveebedrijven te verminderen.

CONCLUSIES

Het management van digitale dermatitis op melkveebedrijven bestaat uit vroege detectie en prompt effectief behandelen van letsels, gecombineerd met het beperken van de transmissie van de infectie binnen het koppel. Tot heden blijft de detectie van digitale dermatitis tijdrovend, in het bijzonder wanneer het frequent gebeurt om letsels in een vroeg stadium te ontdekken. Technieken die computervisie en artificiële intelligentie gebruiken, lijken het meeste potentieel te hebben voor automatische detectie van digitale dermatitis. Langs de andere kant kan men zich afvragen of het niet zinvoller is om te focussen op de automatische detectie van poten met een afwijkende klauwgezondheid, ongeacht het letsel. Dit omdat het merendeel van de oorzakelijke letsels uiteindelijk in een bekapbox behandeld moeten worden en de diagnose van de meeste kreupelheidsaandoeningen het meest nauwkeurig gesteld kan worden in de bekapbox.

De topicale behandeling van digitale dermatitis richt zich momenteel volledig op actieve letsels. Hiermee worden de negatieve effecten op dierenwelzijn en productie zo veel mogelijk beperkt. Desalniettemin resulteren de meeste behandelprotocollen in een transitie naar een chronisch letsel en slechts een minderheid van de letsels geneest naar onaangetaste huid. In het kader van verantwoord gebruik van antibiotica is de topicale behandeling van digitale dermatitis met antibiotica niet wenselijk. Er zijn voldoende niet-antibioticum alternatieven beschikbaar, die minstens even goede resultaten behalen. Ondanks het beperkte wetenschappelijk bewijs ervoor, lijkt het gebruik van verbanden een positief effect te hebben op de genezing van digitale dermatitis.

Het beheersen van digitale dermatitis op koppelniveau bestaat uit het verminderen van het aantal geïnfecteerde dieren door de prevalentie van dieren met letsels te reduceren, transmissie van infectie te beperken door het contact van de poten met mest te minimaliseren en door de vatbaarheid van de dieren voor digitale dermatitis te verminderen door middel van genetische selectie. Om al deze factoren samen te brengen, moeten adviseurs van melkveebedrijven niet enkel over veel kennis beschikken, maar ook goed kunnen communiceren en de veehouder weten te motiveren.

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Stay awkward, brave, and kind.

Brené Brown

Chapter 1

General Introduction

BACKGROUND

Lesions of bovine digital dermatitis were first identified in 1972 by Mortellaro in his veterinary degree thesis under the guidance of Cheli at the University of Milan, Italy. At the time, Mortellaro and Cheli classified the lesions as "dermatite interdigitale del bovine" and recorded a within herd prevalence of 60 to 70% (Mortellaro, personal communication, 2019). During an international meeting to discuss the nomenclature of lesions of the bovine foot, Cheli and Mortellaro became aware that the lesions they had studied were different from interdigital dermatitis (Figure 1.1). Hence, Cheli and Mortellaro (1974) presented their findings as digital dermatitis at the 8th International Conference on Diseases of Cattle in Milan, Italy.

Interestingly, the common term used by farmers and veterinarians in the Netherlands, Belgium, and German speaking countries became "Mortellaro's disease". However, the scientific internationally agreed nomenclature is "digital dermatitis" (Egger-Danner et al., 2020), and will be used in this thesis.

Although digital dermatitis was first described in Italy, it was soon reported globally with the majority of dairy herds in present-day dairy producing countries endemically infected. In Europe, 22 to 99% of the dairy herds studied are reported infected with the majority of studies reporting over

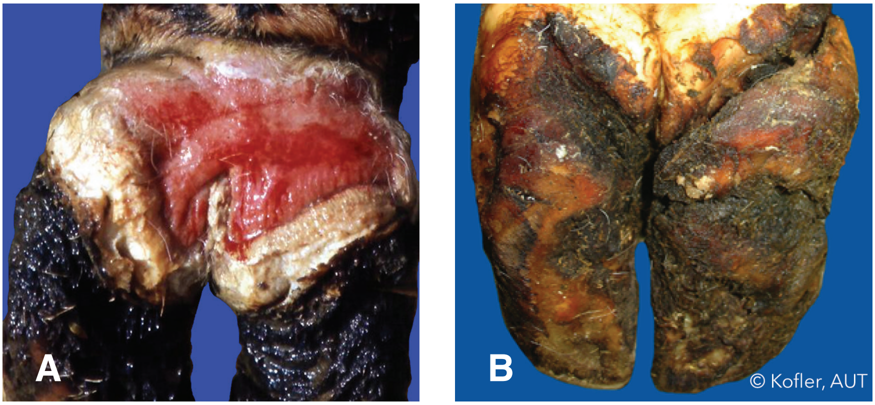

Figure 1.1. Plantar or palmar aspect of bovine feet with (A) a severe digital dermatitis lesion, characterized by ulceration and redness (courtesy of Mortellaro), and (B) an interdigital dermatitis lesion, characterized by V-shaped erosions of the bulb horn – the current internationally agreed nomenclature is "heel horn erosion" (Egger-Danner et al., 2020).

85% of the herds infected (Somers et al., 2003; Holzhauer et al., 2006; Capion et al., 2021; Holmøy et al., 2021; Jury et al., 2021; Pirkkalainen et al., 2021). Within-herd digital dermatitis prevalence in European studies ranged between 3 and 83% (Holzhauer et al., 2006; Aubineau et al., 2021; Holmøy et al., 2021; Pirkkalainen et al., 2021). Regardless of the geographical location of the herd, lesions of digital dermatitis are the leading cause of infectious lameness in dairy cattle, thereby negatively affecting animal welfare and farm economics through production loss, decreased reproductive performance, treatment costs, and increased risk of culling (Bruijnis et al., 2012a; Higginson Cutler et al., 2013; Dolecheck and Bewley, 2018).

ETIOLOGY OF DIGITAL DERMATITIS

Current hypothesis is that digital dermatitis is a multifactorial disease that has a polytreponemal etiology, with *Treponema pedis*, *Treponema medium*, and *Treponema phagedenis* most commonly identified (Orsel et al., 2018; Caddey and De Buck, 2021). Alongside *Treponema*, the genera *Mycoplasma*, *Porphyromonas*, and *Fusobacterium* best differentiate digital dermatitis positive skin from digital dermatitis negative skin (Caddey and De Buck, 2021). What remains unclear, is the exact role of these different bacteria in the pathogenesis of digital dermatitis.

Only a few studies managed to initiate digital dermatitis lesions in cattle (Read and Walker, 1998a; Gomez et al., 2012; Krull et al., 2016a). Best results were achieved using digital dermatitis lesion biopsy macerates for inoculation of pre-conditioned, macerated skin and reduced access to air. While Read and Walker (1998a) concluded pre-existing trauma not essential for lesion induction, the final lesion induction protocol of Krull et al. (2016a) included skin abrasion as a pre-condition. Apart from the cattle model, other strategies used to elucidate the etiology of digital dermatitis are a sheep and murine abscess model (Elliott et al., 2007; Wilson-Welder et al., 2018b; Arrazuria et al., 2020), and studies using digital dermatitis lesion biopsies, human epidermal keratinocytes, bovine foot skin fibroblasts, genomics, proteomics, or a combination of these techniques and animal models (Wilson-Welder et al., 2018a; Nally et al., 2019; Bonacin et al., 2020; Espiritu et al., 2020; Khemgaew et al., 2021; Newbrook et al., 2021; Staton et al., 2021). In general, these studies investigated the host-pathogen interactions related to digital dermatitis at histopathological, immunological, or genetic level. The details from these studies are outside the scope of this thesis and the reader is referred to the original studies for more details.

In conclusion, current consensus is that digital dermatitis is a polymicrobial and multifactorial disease, with skin maceration and reduced access to air considered essential pre-conditions and a fundamental role for *Treponema* spp.. Yet the exact etiology of digital dermatitis remains unclear. In addition, many of the results from fundamental research using non-bovine animal models or in vitro studies, still need to be confirmed in cattle. Together with a lack of digital dermatitis studies using a cattle model to induce lesions, this results in the majority of scientific information on digital dermatitis originating from field trials with natural infections.

DIGITAL DERMATITIS LESIONS

The majority of lesions are seen in lactating dairy cattle, but in infected herds usually a proportion of the dry cows and youngstock are also affected (Laven and Logue, 2007; Capion et al., 2009; Holzhauer et al., 2012; Solano et al., 2016a; Jacobs et al., 2017a). Lesions of digital dermatitis typically affect the plantar or palmar aspect of the pastern region of the foot on the border of skin and horn, with hind feet affected most. Yet, in dairy cattle digital dermatitis has also been associated with pressure sores, hock lesions, ischemic teat necrosis, and digital dermatitis-associated claw horn lesions (Sykora et al., 2015; Clegg et al., 2016a; b; c; Kofler, 2017). Lesions infected with *Treponema* spp. have also been reported in beef cattle, dairy sheep, dairy goats, captive European bison, Mediterranean dairy buffaloes, elk, and pigs (Clegg et al., 2015, 2016d; Crosby-Durrani et al., 2016; Guccione et al., 2016; Gelasakis et al., 2019; Cortes et al., 2021; Hoby et al., 2021). To date, there seems little evidence that non-bovine species play an important role as a reservoir of infection for digital dermatitis in cattle.

Several attempts have been made to develop classification systems for the lesions of digital dermatitis. In brief, Laven and Proven (2000) classified digital dermatitis lesions according to lesion color among other clinical signs; Manske et al. (2002a) classified digital dermatitis lesions according to severity and stage of development; Vink et al. (2009) classified digital dermatitis lesion according to size, clinical presentation, and location; and Krull et al. (2014) classified digital dermatitis lesions according to morphological appearance (Iowa-score). The most commonly used and cited method is the M-score which reflects the on-farm epidemiological lesion progression (Döpfer, 1994; Döpfer et al., 1997). The 'M' stands for "Mortellaro" and the number for disease stage (Figure 1.2). The classical lesion of digital dermatitis is the M2-stage and it is the centrepiece to which the other stages were related during the development of the M-score (Döpfer, 1994). The M1-stage often precedes the M2-stage and is considered the early stage of digital dermatitis. Lesions of the M1-stage are described as a circumscribed granulomatous epithelial erosion, <2 cm in diameter, with redness, a pungent odor, swelling, and pain upon touch. An M2-stage lesion is characterized by ulceration >2 mm below epithelial level and >2 cm in diameter, redness, a pungent odor, swelling, and is often painful causing lameness. The hairs surrounding the lesion are often long, coarse, and upright. The M3-stage is characterized by a dry dark brown to black crust which is not painful. The M3-stage lesions typically can be seen within a few days after topical treatment of the ulcerative lesions. The majority of lesions eventually transition to the M4-stage. The M4-stage is the chronic stage of digital dermatitis and presents itself as a brown to black rubbery hyperkeratotic lesion. Within these M4-stage lesions, sometimes small ulcerative areas, reflecting M1-stage lesions, develop. This resulted in the addition of the M4.1-stage lesion to the M-score by Berry et al. (2012). Normal unaffected skin is classified as M0 (Berry et al., 2012). Within the M-score classification, lesions can be grouped as early (M1), infectious (M2 and M4), or healing (M3) (Döpfer et al., 2012) and as active (M1, M2, and M4.1) or inactive (M3 and M4) by (Zinicola et al., 2015b; Biemans et al., 2018). Any lesion of digital dermatitis can also be proliferative and

Figure 1.2. (Right page) Digital color photographs of hind feet from dairy cattle with different M-scores of digital dermatitis lesions: M0 top left, M1 top right, M2 middle left, M3 middle right, M4 bottom left, and M4.1 bottom right (Kofler et al., 2019).


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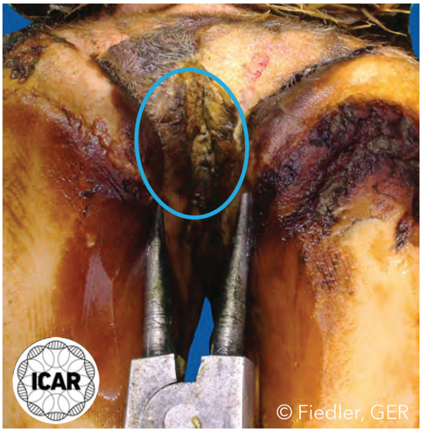
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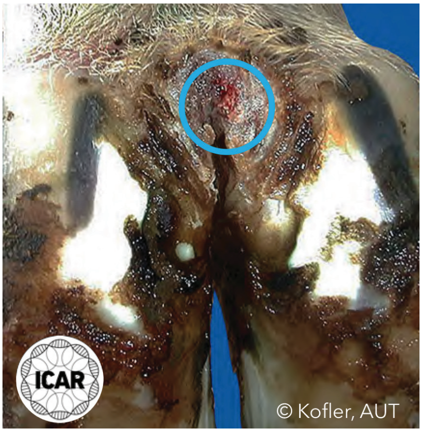
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thereby raised above normal skin level. While the M-score was designed as a reflection of logical lesion progression from M1 to M2, over M3, to M4, current understanding is that a mixed pattern of transitions is possible (Figure 1.3).

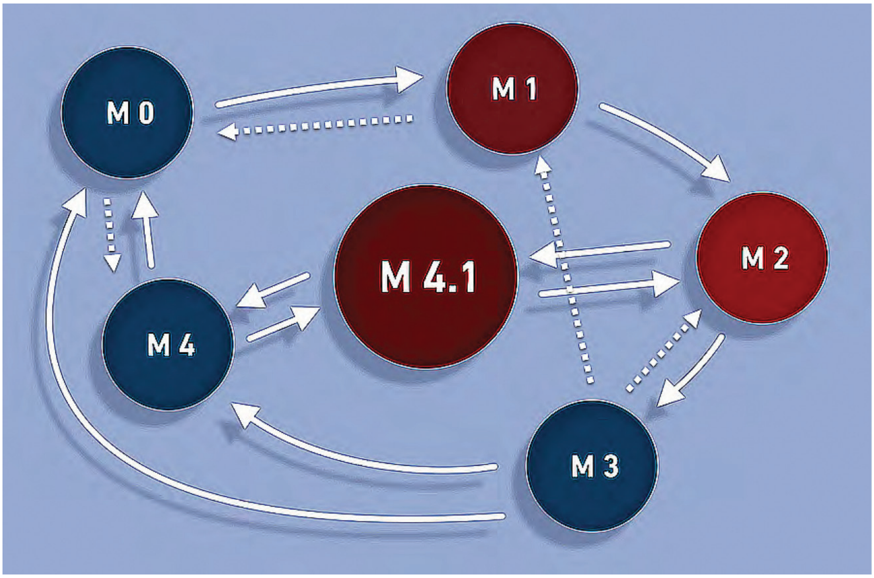

Figure 1.3. Possible M-score transitions of digital dermatitis lesions, modified from Kofler et al. (2019). Solid arrows indicate very likely transitions, dotted arrows indicate less likely transitions, red circles represent active stages, and blue circles represent chronic stages including healthy skin (M0-stage).

A remarkable aspect of digital dermatitis lesions is that after initial lesion improvement following topical treatment, a substantial amount of lesions demonstrate recrudescence to more severe lesion stages. Using several treatment approaches varying between systemic or topical antibiotic treatment, topical caustic treatment, and surgical excision, Read and Walker (1998b) reported lesion recrudescence in 13 of 51 (26%) treated lesions during a follow-up period of 49 to 84 days. Berry et al. (2012) reported lesion recrudescence in 21 of 39 (54%) lesions treated with topical lincomycin within a 341 day follow-up period. In their study, the earliest recrudescence appeared at 38 days post treatment and eight (21%) lesions recurred more than once with a maximum of five times. Likewise, Krull et al. (2016b) reported lesion recrudescence in 20 of 43 (47%) lesions treated with topical oxytetracyclines during a follow-up period of minimum 50 days. Gomez et al. (2015) followed a cohort of 719 pregnant heifers from a single herd for six months until their first calving and classified them according to the number of M2-stage lesions identified during this period, with 458 (64%) heifers where no M2 lesions were identified (type I animals), 136 (19%) heifers where a single M2 lesion was identified (type II animals), and 125 (17%) heifers where two or more M2 lesions were identified (type III animals). What remains unclear is whether these recurring lesions are the result of reactivation of *Treponema* spp. in the dermis of the initial digital dermatitis lesions or if they are new infections originating from *Treponema* spp. in the environment.

IMPACT OF DIGITAL DERMATITIS IN DAIRY CATTLE

Pain and Lameness

In general, active lesions are reported to be painful (Kofler et al., 2004; Higginson Cutler et al., 2013; Paudyal et al., 2020; El-Shafaey et al., 2021; Kasiora et al., 2022), with M2 lesions considered most painful (Holzhauer et al., 2008; Schultz and Capion, 2013). It is important to note that Higginson Cutler et al. (2013) reported not only active, but also healing lesions of digital dermatitis to be painful. They defined healing lesions to be dry and developing a scab. They also reported a large degree of variation in nociceptive thresholds for active lesions. Of the feet with active lesions tested in their study, 50% had withdrawal responses at three kg or less of force and almost 20% tolerated the maximum force of 25 kg, like unaffected feet in their study. This variation in nociceptive thresholds was also reported by Holzhauer et al. (2008) with 42% of the M2 lesions in their study having a pain response to firm pressure with one thumb (± 50 N / cm^2). These findings suggest that all lesion of digital dermatitis can be painful, but that the level of perceived pain varies between lesion stages and cows.

As a result of the differences in pain associated with lesion stages and nociceptive thresholds in cattle, the degree of lameness related to digital dermatitis lesions varies greatly among studies, ranging between 2 and 80% (Kofler et al., 2004; Capion et al., 2009; Frankena et al., 2009; Tadich et al., 2010; Schulz et al., 2016; Sadiq et al., 2017; Hässig et al., 2018; Moreira et al., 2018b; Sellera et al., 2021; Kasiora et al., 2022). A few studies highlight specific aspects of the association between digital dermatitis and lameness. Following topical treatment of digital dermatitis lesions, cows on average remain lame for 2.4 weeks (Schulz et al., 2016). The addition of a non-steroidal anti-inflammatory drug to the treatment of active digital dermatitis lesions in lame cows, decreased the odds to remain lame one week post treatment (Kasiora et al., 2022). In tie stalls, digital dermatitis lesions result in weight shifting (Jewell et al., 2021), a clinical sign often described as cows standing on tiptoes, which is also seen while cows are in the milking parlor or at the feed rail.

Reproductive Parameters

Cows that have digital dermatitis and are lame, are less likely to conceive when compared with healthy counterparts (Hernandez et al., 2001). Gomez et al. (2015) reported pregnant heifers that experienced multiple digital dermatitis events during the six months rearing period until their first calving to have lower conception to first service rates and increased number of days open in their first lactation when compared with pregnant heifers that remained free from digital dermatitis during the six months rearing period until their first calving. De Jesús Argáez-Rodríguez et al. (1997) identified cows with digital dermatitis to have lower conception rates in the first 90 days postpartum and more days open than cows without digital dermatitis. Yet, this did not translate into differences between cows affected with digital dermatitis and cows without digital dermatitis in the proportion of pregnant animals at the end of the follow-up period, the average number of services to conception, and the calving interval in the study period.

Milk Production

The majority of studies investigating the effect of digital dermatitis on milk yield report production losses varying from 0.5 to 7.2 kg / infected animal / day in endemic herds, when compared with unaffected counterparts (Yeruham et al., 2000; Pavlenko et al., 2011; Relun et al., 2013c). In primiparous animals, higher milk losses were associated with moderate lesions, whereas in multiparous animals highest losses were described for severe lesions (Relun et al., 2013c). The effect on milk production is likely caused by the discomfort associated with digital dermatitis lesions. Due to the chronicity and high recurrence rate of digital dermatitis lesions, infected animals have lower 305-d (199 to 335 kg) and lifetime (3,513 kg) production (Gomez et al., 2015; Randall et al., 2016). Others reported lower yields in cows with digital dermatitis, yet this difference was not significant (De Jesús Argáez-Rodríguez et al., 1997; Hernandez et al., 2002). Possible reasons for these non-significant results were a lack of power in the study or positive response to treatment. The latter was confirmed by Amory et al. (2008), who reported a higher milk yield following treatment when compared with the milk yield before treatment, but not when compared with non-lame animals. They also reported a lower milk yield prior to treatment of digital dermatitis lesions and a slight increase in milk yield immediately after treatment when compared with unaffected animals. Few studies also looked at the effect of digital dermatitis on milk constituents and reported no differences in milk fat and protein (Pavlenko et al., 2011; Gomez et al., 2015).

Culling

Based on retention payoff, Cha et al. (2010) modelled the moment to cull an open, non-pregnant lame cow with digital dermatitis to be one month earlier than for an open, healthy cow. When milk production dropped below herd average, this difference in moment to cull between open lame cows with digital dermatitis and open, healthy cows enlarged.

Costs[1]

Costs of animal diseases comprise losses and expenditures. Applied to digital dermatitis, losses consist of decreased milk production, reproductive failure, and culling, whereas expenditures are made up from expenses for time and products needed for treatment and prevention. Different studies included different cost components, assumptions, farm characteristics, and farming systems making comparisons on costs difficult among studies. The only Dutch study on costs of digital dermatitis is by Bruijnis et al. (2010). They modelled the costs of digital dermatitis on a typical Dutch dairy herd in 2008 with a mean milk production of about 8,500 kg / year and calving interval of 415 days from 65 cows in cubicle housing with slatted concrete floor, pasturing during summer, and two whole herd foot trimming interventions per year associated with the beginning and end of pasturing. Incidence of digital dermatitis cases per 100 cows per year were modelled to be 27% and 20% for subclinical and clinical, respectively. Yearly costs of digital dermatitis on their modelled farm averaged just over 1,000 EUR, with about 80% of these costs originating from clinical cases. Reported costs per case of digital dermatitis vary between 52 and 96 EUR (Willshire and Bell, 2009; Cha et al., 2010; Dolecheck et al., 2019). In a survey among dairy hoof care professionals in the USA, mean treatment costs per case of digital dermatitis was 6.09 EUR with 65% of the costs attributed to labor and 35% to supplies (Dolecheck et al., 2018). For comparison, reported costs of a case of white line disease or sole ulcer, the two other most common lesions causing lameness in dairy cattle, are at least double those of a case of digital dermatitis.

[1]All costs have been converted to EUR using historical conversion rates from the submission date of the publication (https://www.xe.com/currencytables/).

Conclusion

All lesions of digital dermatitis can be painful with the degree of perceived pain varying between lesion stages and cows. This discomfort, especially when resulting in lameness, is likely to alter the behavior of infected animals and is the underlying mechanism associated with decreased reproductive performance and production losses. Although lower than for white line disease and sole ulcers, costs related to digital dermatitis can be significant, especially in herds with high prevalence or incidence of active lesions.

MANAGEMENT OF DIGITAL DERMATITIS IN DAIRY CATTLE HERDS

Management of digital dermatitis in dairy herds is achieved at two levels. First, there is a need to control infection pressure within the herd. This is typically done using biocide containing footbaths together with other management practices, in general related to foot hygiene. Second, there is the need to treat painful lesions to warrant animal welfare and reduce production losses. Many of the aspects of current digital dermatitis control are labor-intensive, expensive, detrimental for the environment, pose a health-risk for the farm-worker, or a combination of these. With the exception of one case report (Yeruham and Perl, 1998), these intensive control programs however do not eradicate digital dermatitis from herds, but at best result in achieving a manageable state of the disease, with the best dairy herds having less than 10% of cows affected (Döpfer and Bonino Morlán, 2008; Bell and Vanhoudt, 2020).

OUTLINE AND AIM OF THE THESIS

Chapter 2 of this thesis provides an overview of the status quo on management of digital dermatitis on dairy herds (Bell and Vanhoudt, 2020). Based on literature and expert opinion, the identification of animals eligible for treatment, treatment strategies, and herd level control through footbaths is reviewed. The next chapters in this thesis describe four applied field studies that were carried out to enhance the scientific evidence related to the management of digital dermatitis: two studies on diagnosis, one on the treatment of active lesions, and one on herd level control.

Diagnosis of Digital Dermatitis

The identification and classification of digital dermatitis lesions is not straightforward due to their anatomical location and the various aspects in which lesions present themselves. Currently, the M-score remains the most widely used, researched, and cited method (Döpfer et al., 1997; Berry et al., 2012). For any classification system to be valid, its users need to be able to assign the same score to the same lesion, each time the lesion is scored. This is often expressed as intra- and interobserver agreement and determines the validity of published research using the classification system. In Chapter 3 we assessed the interobserver agreement of the M-score by unstandardized, independent, experienced scorers, using single, digital color photographs of standing dairy cattle hind feet (Vanhoudt et al., 2019).

To date, inspection of the feet in a foot trimming chute is considered best practice for the diagnosis of digital dermatitis. This practice is labor-intensive and despite good cattle handling, cows often experience a degree of stress during the procedure (Pesenhofer et al., 2006; Janßen et al., 2016; Heinrich et al., 2020). Alternatively, screening for digital dermatitis in the milking parlor, at the feed rail, or during pen walks has been validated with varying but often mediocre test characteristics (Relun et al., 2011; Stokes et al., 2012a; Solano et al., 2017a; Cramer et al., 2018). To enable automated detection, efforts were made using infrared thermography or computer vision and machine learning (Stokes et al., 2012b; Alsaaod et al., 2014; Cernek et al., 2020). In Chapter 4 we tested the association between skin temperature measured by infrared thermography and the presence of M2 lesions under farm conditions, with the ultimate goal of automated lesion detection (Vanhoudt et al., 2023).

Treatment of Lesions and Control of Digital Dermatitis

A plethora of products for topical treatment of digital dermatitis lesions were studied, with most having an antimicrobial component. Whether or not these products should be applied under a bandage is still the topic of much debate, with current evidence in favor of bandaging (Higginson Cutler et al., 2013; Klawitter et al., 2019; Alsaaod et al., 2022). The majority of these topical treatments mitigate the pain associated with digital dermatitis lesions, but fail to achieve cure, i.e. return to unaffected skin, in a substantial number of lesions. In Chapter 5 we investigated the effect of two non-antibiotic gels under bandage on hind feet with active digital dermatitis lesions in dairy cattle (Vanhoudt et al., 2022). Treatment effect was assessed using the M-score and wound healing progress criteria.

Many studies identified risk factors and control measures associated with digital dermatitis variation between herds (Potterton et al., 2012; Palmer and O'Connell, 2015; Cook, 2017). Particularly factors related to foot health and housing management can potentially be adapted by a farmer to facilitate digital dermatitis control. In Chapter 6 we utilized an available checklist based on reported risk factors (van Huyssteen et al., 2020) to carry out farm specific risk assessments, with the aim to raise awareness of the digital dermatitis prevalence and to provide the farmer and the veterinarian with specific control options (Vanhoudt et al., 2021).

Chapter 7 concludes this thesis with a general discussion providing a reflection on insights gained and suggestions for future research on the diagnosis, treatment, and control of digital dermatitis in dairy herds.

Chapter 2

Treating and Controlling Digital Dermatitis in Dairy Cattle

Bell, N., and A. Vanhoudt. (2020) Treating and controlling digital dermatitis in dairy cattle. In Pract. 42:554–567. doi:10.1136/inp.m4454.

BACKGROUND

Digital dermatitis is one of the main causes of lameness in dairy cattle, and is prevalent in most dairy herds worldwide and is of major welfare and economic significance.

AIM OF THE ARTICLE

This article focuses on current concepts of digital dermatitis treatment and control strategies, but will not go into detail about most concepts relating to prevention – namely biosecurity, improving foot hygiene, nutrition, and genetics. The article includes concepts related to disease screening, treatment at both an individual cow level and with footbaths, and the control of digital dermatitis through foot disinfection using footbaths. Readers are referred to other detailed reviews where appropriate, such as Plummer and Krull (2017) and Orsel et al. (2018).

INTRODUCTION

Digital dermatitis is reported in most dairy producing countries worldwide. It is prevalent in the majority of UK dairy herds, affecting 15 to 41% of cows on average (Somers et al., 2005; Holzhauer et al., 2006; Vink, 2006; Stokes, 2011; Solano et al., 2016a), although there are no reliable recent estimates. It is one of the main causes of lameness in dairy cattle, contributing to many primary and secondary lesions, such as interdigital skin hyperplasia and chronic necrotic claw lesions (e.g., toe necrosis).

Consequently, digital dermatitis has major welfare and economic significance, with the costs per clinical case estimated to be between £53 and £76 (Willshire and Bell, 2009; Dolecheck et al., 2019), although costs of subclinical and secondary disease have never been well established.

CAUSE OF DIGITAL DERMATITIS

Digital dermatitis is a polymicrobial infection, with temporal changes identified in microbial species as the lesions progress. Metagenomics studies have highlighted the involvement of many hundreds of microbial species in digital dermatitis infections (Zinicola et al., 2015a) – several treponemes have been consistently found in digital dermatitis lesions, and these are capable of reproducing disease in induction experiments (Gomez et al., 2012).

Three species of treponeme are regularly found – *Treponema medium*, *Treponema phagedenis*, and *Treponema pedis*. Treponemes are found in greatest abundance when invading the dermis via hair follicles and sebaceous glands (Evans et al., 2009). However, they have been difficult to isolate in the environment, except on hoof-trimming equipment and in the footprints formed in slurry by infected cows (Bell, 2017; Gillespie et al., 2020a). Indeed, treponemes appear to persist in the dermis in spite of clinical recovery (Berry et al., 2010). This suggests that they are able to evade the immune system, making the likelihood of a future vaccine challenging.

Moreover, although treponemes are fastidious anaerobic spirochetes, meaning they cannot survive for long periods of time in a clean environment, there is an encysted form which allows persistence for longer than previously realised. This encysted form is difficult to isolate by standard laboratory techniques.

While the majority of dairy cattle are susceptible to digital dermatitis, many never experience an infection. However, recent research into short nucleotide polymorphisms that can be used to predict resistance or susceptibility to infection makes this disease an obvious candidate for genomic selection (Scholey et al., 2010; Biemans et al., 2019a).

Furthermore, the observation that foot lesions in cattle are the main source and reservoir of infection suggests that control measures should focus primarily on treatment and biocontainment of animals with non-regressing lesions, and also the protection of uninfected animals with good foot hygiene, cleaning, and disinfection protocols.

THE M-SCORE

Various digital dermatitis grading and scoring systems exist, with the simplest and most reliable system involving recording the presence or absence of a digital dermatitis lesion. A popular and widely used scoring system is the M-score (Figure 2.1), which identifies six epidemiologically significant lesion categories (M0 to M4.1; Döpfer et al., 1997; Berry et al., 2012). The most common lesion category is the chronic hyperkeratotic or proliferative lesion (M4). Lesions at this stage, particularly the proliferative type, are most likely to drive epidemics due to the speed and rate with which they can reactivate (to a score of M4.1) and also due to their ability to return to the ulcerated stage (M2) (Biemans et al., 2018). Triggers for reactivation could include immunosuppression (e.g., calving, stress, bovine viral diarrhea infection, or other concurrent disease), challenging underfoot conditions (wet, unhygienic conditions), or failures in footbathing regimes. In these circumstances, the M4 lesion can reulcerate within a

Figure 2.1. (Right page) Digital color photographs of hind feet from dairy cattle with different M-scores of digital dermatitis lesions: M0 top left, M1 top right, M2 middle left, M3 middle right, M4 bottom left, and M4.1 bottom right (Kofler et al., 2019).


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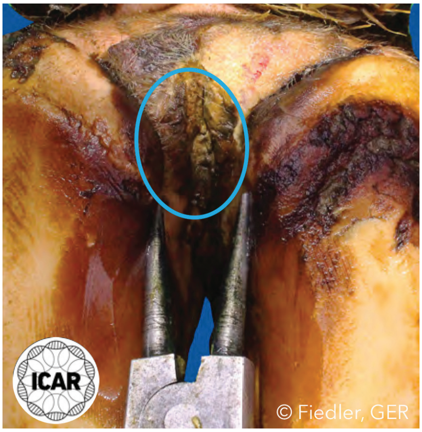
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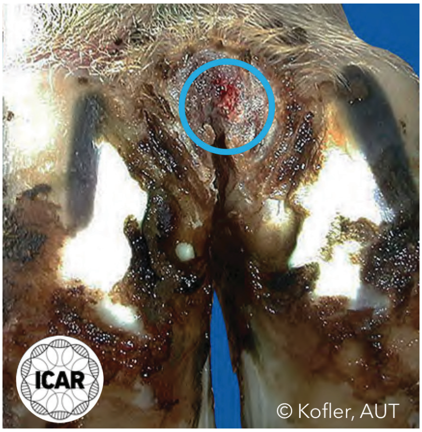
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matter of days, rather than the typical timeframe for new infections which is usually many weeks [e.g., Krull et al. (2016b) reported the timeframe to be 133 days].

The M-score was originally applied to inspections in lifted feet; however, more recently it has been adapted for screening in parlors and standing animals. For full guidance on the M-score, readers are referred to the ICAR guide (Kofler et al., 2019). Furthermore, it is important to note that the M-scores do not represent a linear progression or severity scale, but are a way of capturing epidemiologically significant lesion stages.

IDENTIFYING ANIMALS FOR TREATMENT

Screening Methods

Screening herds for lesions and subsequently treating them can be an effective way to control digital dermatitis. Surveys have found over 30% of animals have lesions in endemically infected herds that do not have effective prevention and control measures in place (Stokes, 2011). These animals often have multiple limbs affected, which can make individual treatment in a foot crush a logistical challenge, even for an average-sized herd. Nonetheless, checking the whole herd and treating all visible lesions in a crush has been adopted by some farms – it has been named the ‘blitz digital dermatitis treatment’ when applied in all age groups at one point in time (Pedersen, 2019).

A popular screening approach is the ‘bright light and sharp jet’ method, which involves hosing feet with water in the milking parlor. This helps to visualize lesions or elicit a pain response as the affected cows shake their feet. Moreover, the use of a mirror or borescope can aid lesion identification in the heel bulb pocket or interdigital space in standing animals (Figure 2.2).

Observing the feet of cattle as they stand along the feed barrier (‘pen walks’) can be used for robotic or automatic milking systems, beef animals, and youngstock groups, provided feet and conditions are clean and bright enough to spot lesions.

Inspecting all animals in the foot crush (e.g., as part of a 'whole-herd check, treat, and trim') could be another approach to screening for lesions.

Typically, the majority of affected cows will have M4 or M4.1 lesions. However, in uncontrolled situations, over 10% of milking cows can have active M1 or M2 lesions, and with this there may also be an increase in related conditions, such as interdigital skin hyperplasia (Manske et al., 2002b).

At the time of writing, there are three digital apps available for the electronic recording of digital dermatitis – DD Check, VetIMPRESS, and Provita Digital Dermatitis.

Identifying Treponemes

Treponemes have also been found in a variety of other skin lesion locations, including hock sores, toe necrosis, sole ulcers, chronic white line infections (wall ulcers), foul-in-the-foot infections, interdigital skin hyperplasia, ulcerative mammary dermatitis, and ischaemic teat necrosis. Treating these lesions will help reduce overall infection pressure.

If treatment fails, culling should be considered in order to reduce the animal reservoir of infection. Lesions, once termed 'non-healing' (i.e., chronic white line lesions, sole ulcers, and toe necrosis), can respond well to surgical debridement under local anesthesia if they are caught early enough (Bell and Mahendran, 2017), and their treatment should be included in a whole-herd digital dermatitis control strategy.

Figure 2.2. Using a mirror glued to a spatula can be a helpful aid for the identification of digital dermatitis lesions in the heel bulb pocket or interdigital space in the standing animal.

INDIVIDUAL ANIMAL TOPICAL TREATMENT

Wound Management

All digital dermatitis lesions should be treated in some way. The first priority of digital dermatitis wound management is to clean, dry, and debride the lesions, followed by the application of an effective antibacterial product. Hygienic debridement of the lesion is essential, using teat wipes, gauze swabs, dedicated hoof knives, or scalpels to remove exudate and dyskeratotic or necrotic material. Local anesthetic is also needed for the surgical debridement and debulking of proliferative lesions.

The goal of wound management is to stimulate a brief but vigorous acute inflammatory response in order to create a healthy contracting granulation tissue bed. This results in full skin thickness wound contraction from early on in the wound healing process – wound contraction minimizes the area that requires re-epithelialization and reduces scarring. There are a variety of wound dressings available; we use Melolin gauze swabs (for a severe or necrotic M2 lesion), or polyurethane (for wet conditions).

In most cows there is a small pocket formed between the heel bulbs; many infections often extend into this pocket so it should be cleaned out regularly. A hose or disinfectant wash (e.g., 1% povidone iodine) can achieve this quickly and effectively, as can a gauze swab drawn through the interdigital space with a finger. Any topical treatments that are used need to penetrate into the interdigital pocket, and using spreading pliers may help to achieve this (Figure 2.3).

Moreover, a 'spray-dry-reapply' routine can raise the local concentration of the active component of the treatment being used. If trimming is being done, then spraying before and after trimming can allow for a sufficient drying time between applications.

Non-Antibiotic Treatments

There are a number of non-antibiotic products available, although only one product – Intra Hoof-fit Gel (Intracare) containing chelated copper and zinc – is currently licensed for digital dermatitis treatment in cattle in the UK. Indeed, this chelated copper and zinc gel and spray has been found to be as efficacious as topical antibiotic treatments (Holzhauer et al., 2011; Dotinga et al., 2017; Klawitter et al., 2019).

Salicylic acid has also become a popular topical treatment worldwide, and there are now licensed products for individual cow treatment in many countries (although currently not in the UK, but salicylic acid is a licensed biocide). Salicylic acid has keratolytic properties and in a Danish study, 10 g of salicylic acid was found to achieve better cure rates (the lesion scores return to a score of M0) than those offered by topical antibiotic treatments (Schultz and Capion, 2013). Furthermore, treponemes do not appear to survive at a pH lower than five, so the acidic nature of salicylic acid is likely to be bacteriocidal (Bell, 2017). However, salicylic acid can be painful when applied directly to ulcerated lesions and the rationale for its use is therefore clearest for hyperkeratotic and dyskeratotic lesions.

Figure 2.3. Spreading pliers are used to visualize the interdigital space and pocket. This needs to be thoroughly cleaned and treatment should be applied to any digital dermatitis lesion.

Antibiotic Treatments

Currently there are no licensed topical antibiotic treatments containing macrolides or penicillins, to which treponemes are most sensitive. It is likely that the polymicrobial nature of the typical digital dermatitis lesion means the UK licensed topical antimicrobial treatments that contain broad-spectrum tetracyclines or thiamphenicol are just as efficacious in practice.

Off-label use of tylosin powder could be justified under the cascade for refractory lesions; however, it carries the minimum statutory withdrawal periods (at least 28 days for meat and seven days for milk, starting from the end of treatment). It is also important to note that a single treatment using 10 g tylosin in soluble powder form contains 50 times the antimicrobial content (mg) of a single oxytetracycline spray treatment.

Injectables. While injectable antibiotics are likely to be efficacious, they are unnecessary for the treatment of uncomplicated digital dermatitis lesions which are caused by dermal and epidermal infections. Indeed, there would be little benefit of using injectable antibiotics in these instances and doing so should be considered overuse.

If injectable treatments are indicated (e.g., a severe ascending infection), then macrolides and penicillins are the treatments of choice. Cephalosporins (cefalexin and ceftiofur) have also shown good efficacy in the field. Moreover, non-steroidal anti-inflammatory drugs can be used due to the pain and swelling involved, and have a beneficial effect on milk yield (Kasiora et al., 2022).

Bandages

Opinions are deeply divided on the use of bandages for the treatment of digital dermatitis. The evidence base for bandaging is surprisingly weak, but overall it is currently in favor of the use of bandages. One trial showed a non-significant trend towards better cure rates with a bandage (Higginson Cutler et al., 2013) and another trial showed a doubling of the cure rate with repeated bandaging (Klawitter et al., 2019).

The purpose of the bandage could be to keep the treatment products in place for a sufficient period of time to allow them to work, but also to maintain a clean, oxygenated, and slightly moist environment for the granulation and re-epithelialization of the wound.

Without bandages, topical digital dermatitis treatments may be removed by bedding material, washed off with footbaths, or removed by slurry. Subsequently, treated lesions can become reinfected if the infection pressure is high (e.g., in wet, unhygienic underfoot conditions). The bandage could also provide a biocontainment barrier to reduce the risk of cross-infection and protect the recovering lesion from chemicals and materials in the farm environment (e.g., lime, sawdust, sand, and formalin). Likewise, the bandage may offer some physical protection to reduce trauma-related pain.

Ensuring treated lesions remain clean and moist (but not wet) would appear to be the most critical element to post-treatment wound management and optimizing four-week cure rates. This is challenging under standard dairy farm conditions, but could be achieved in different ways. For example, in a German study, a four-layer waterproof bandage that was applied weekly for four weeks roughly doubled the cure rate, although, no footbathing or grazing was conducted during this study (Klawitter et al., 2019). Regular footbathing or repeated washing of the feet with water or soap may be an alternative way to achieve this (Jacobs et al., 2018).

If conditions make bandages wet they should be replaced or removed – under standard farm conditions with footbathing or grazing, a gauze or melolin dressing held in place with a standard Vetrap (3M) bandage becomes wet within two days. It might be possible to use techniques to maintain dry bandages for several days, but this may be unrealistic in most farm conditions involving regular (daily) footbaths. Some treatments, such as aluminium wound sprays or copper pastes, may have some intrinsic barrier properties to reduce the risk of reinfection, but these remain clinically unproven.

A worthy compromise may be the use of the ‘bikini wrap’, which is a very light, figure-of-eight dressing technique, applied for eight to 12 hours to allow sufficient time for the treatment to remain on the lesion. These wraps are then removed at the next time of milking, if they have not fallen off already. However, they do not protect the healing wound from environmental conditions for long periods of time.

Further work is needed to establish a reliable way to apply non-occlusive (breathable), water-repellent dressings practically in the field, as well as principles for deciding the minimum period of time that a dressing is needed. For example, in other species, including people, bandages are advised to be kept on wounds until full wound closure is achieved.

For most clinicians and professional foottrimmers, the greatest concern regarding bandaging is the dressings remaining on for too long. Bandage injuries can occur if removal is missed and the bandage then cuts into the limb, compromising the blood supply to the foot and leading to ischaemic necrosis. Likewise, prolonged moisture held on a foot with a wet or occlusive bandage can macerate skin, in turn reducing the rate of healing, compromising cure rates, and predisposing the animal to new infections such as foul.

Bright bandage materials are recommended (vibrant blue is conspicuous), as is a protocol for checking and removing the bandage with a long-handled bandage knife at a set time following a specific treatment session. To ensure these protocols are followed, management software can be programmed to generate lists of cows that require bandage removal. However, the complexity and labor cost associated with these sorts of protocols means that for some farms, long-term and sustainable treatment protocols are better off being simplified to exclude the use of bandages, and they should therefore accept some reduction in cure rate.

Bandage Powders and Gels. The use of powders and gels generally require a bandage to hold the active agent in place. While a bandage may improve wound healing, it is important to note that none of the licensed antibiotic sprays require a bandage, and that the repeated reapplication of antibiotic treatments is likely to improve infection cure rate.

Consequently, for farms with good yard hygiene and poor bandage management, focusing on compliance with repeat treatments will be more important. Follow-up treatments could involve products administered at milking time, such as copper spray (e.g., Intra Hoof-fit Spray; Intracare) or 1% povidone iodine.

Hygiene Practices

Given that there is a risk of disease transmission during treatment, consistent hygienic practices and equipment disinfection should be performed to minimize cross-infection to other limbs or other cattle coming through the handling system or foot crush. For example, keeping the working area clean and washing the cow's feet with disinfectant will help. Likewise, keeping knives and gloved hands disinfected between active cases should all be part of best practice – blades used to debride a digital dermatitis lesion should never be used on other feet or lesions without disinfection beforehand, despite this slowing down the trimming process (which comes at a considerable cost to professional foottrimmers).

Most disinfectants appear to be effective, but 1% FAM30 (Quill Productions), 2% Virkon (Lanxess), or 2% hypochlorite are particularly effective (Gillespie et al., 2020a). The most cost-effective means of disinfecting feet could be to run cows through a footbath immediately after treatment, although this should be avoided for cows with open digital wounds or bandages.

FOOTBATH TREATMENTS

The off-label use of antibiotic footbaths under the cascade is no longer justifiable and they have been superseded by other, more effective approaches (Bell and Main, 2011; Bell et al., 2017). Antibiotic footbaths contribute to a high proportion of antimicrobial use (Hyde et al., 2017), and are considered a risk for antimicrobial resistance on farm as they do not satisfy the modern standards of responsible antimicrobial use. This is particularly apparent regarding disposal, as this involves discarding the antibiotic footbath solution into slurry lagoons. While clinical improvement is observed using footbaths (there is a reduction in pain and ulceration), cure rates (i.e., lesions returning to a score of M0) are generally poor compared with other treatment strategies (Laven and Hunt, 2002). Furthermore, the minimum statutory milk and meat withdrawal periods make these treatments untenable for dairy producers.

Some non-antibiotics, such as formalin and organic acids, have been used for whole-herd treatments; however, the efficacy of these compared to targeted individual animal treatment with topical licensed products is questionable. Formalin and organic acids act as surface disinfectants and both have a low, acidic pH. This means that formaldehyde reacts with amines groups, chemically cauterizing the wounds. Whether this chemical cauterization of small lesions with biocidal treatments is beneficial is unclear – the current consensus is that it is harmful for larger M2 lesions, but beneficial for the more superficial M1 lesions (and M4.1 lesions).

In endemically infected herds with high disease prevalence, particularly those with a large proportion of M1 lesions, it may be prudent to start by hosing the feet clean in the parlor before segregating the cows with M2 lesions for individual treatment and walking the remainder of the herd through a footbath.

Historically, copper sulphate baths were used, but this is no longer an EU-approved biocide for use on animals (Box 2.1). A rising concentration of formalin may be adopted (Table 2.1), but it is important to be aware that this can cause pain for cows that have ulcerated lesions. This makes the segregation of cows with M2 lesions for treatment very important for their welfare. It is also important to note that there is an increased risk of chemical burns at higher concentrations in warm and windy conditions.

A similar treatment outcome may be achieved by using an organic acid solution (e.g., 5% Hoofsure Endurance; Provita) but again caution must be applied as chemical burns are possible at high concentrations (>5%). Nevertheless, establishing and sustaining an effective foot disinfection regime is an important consideration for the period following any herd treatment (by whatever means) to prevent immediate reinfection – footbathing with an appropriate biocide needs to be discussed at the outset.

Formalin is less volatile than water, so in windy, drying weather conditions, it can concentrate on the limbs, giving rise to a risk of chemical burns. At lower temperatures, biocidal activity appears to be reduced, but once the product comes into contact with the cow's limb it achieves an optimal temperature within a few seconds.

BOX 2.1. EU BIOCIDES LEGISLATION

The regulation of chemicals for foot disinfection falls under EU legislation. This is enforced through national bodies such as the Health and Safety Executive. The relevant EU legislation includes:

- Biocidal Products Regulation (Regulation (EU) No 528/2012)
- Biocidal Products Directive (Directive 98/8/EC)

Approved applications are then referred to the European Chemical Agency (ECHA). The ECHA maintain a list of approved biocides for skin disinfection which fall under category PT3 (veterinary hygiene) listed in article 95 (see further resources). Approved biocides exclude copper sulfate, but some examples of the approved biocides relevant to the control of digital dermatitis are listed below (approved at the time of writing):

- formalin (37% formaldehyde)
- glutaraldehyde
- peracetic acid
- formic acid
- salicylic acid

The use of formalin is governed by strict legislation due to its probable carcinogenic status. Strict limits of 2 ppm (moving to 0.3 ppm) formaldehyde exposure will be enforced across the EU and this would need to be monitored by farmers using commercially available meters. Persons who are handling formalin must be competent (trained) and equipped with suitable personal protective equipment, including eye protection, overalls, respirators, and gloves. It is the responsibility of the farmer to ensure the appropriate legislation is adhered to.

Table 2.1. Footbath treatment regimes used to control M1, M4, and M4.1 lesions

Footbath biocide	Regime
Rising formalin regime (R. Blowey, personal communication)	Exclude cows with M2 lesions – treat these individually in the crush. Solution should be replaced once daily for three consecutive days per week: Week 1: 2% formalin Week 2: 4% formalin Week 3: 6% formalin Week 4: 8% formalin[1] Week 5: 10% formalin[1] Week 6: 3–4% formalin three to seven days per week as part of routine foot disinfection
Organic acid protocol	Individually treat animals with M2 lesions. 5% Hoofsure Endurance (Provita) footbaths should be used day and night milking for three consecutive days in a week. Repeat weekly as needed to achieve control.

Regular foot disinfection with formalin can maintain M4 lesions in that state.
[1]Note this can cause chemical burn in warm, drying (windy) conditions and so this stage should be skipped if there is a risk.

Whenever advocating the use of formalin, it is important to advise that it is a probable (Class 1b) carcinogen and should be handled in accordance with national legislation. At the time of writing, under UK law this means handling should be performed by those who are competent (trained) and wearing the appropriate personal protective equipment. Moreover, for all footbaths it is important to carefully calibrate the volume of bath and chemical being added. Just performing estimates based on filling levels in footbaths can be prone to large errors (Holzhauer et al., 2004).

FOOT DISINFECTION (ROUTINE FOOTBATHING)

Cross-Infection

The majority of new digital dermatitis infections are likely to arise through an uninfected cow treading in a spot where an infected cow had recently been, with cross-infection occurring via a contaminated footprint (Bell, 2017), and dermal colonization via the hair follicle (Evans et al., 2009). Prevention strategies that focus on minimizing the risk of cross-infection via footprints may be effective, but exposure is inevitable due to cows congregating during milking, feeding, and penning for other routines.

A high prevalence of M4 lesions should be noted as requiring improvements in digital dermatitis management or the need for better footbathing protocols – the best herds maintain levels of non-regressing lesions (M1, M2, M4, and M4.1) below 10%, and M1 or M2 lesions below 1%.

Clean and dry feet appear to be the most resistant to infection. In general, extended grazing, loose straw yards, or modern sand cubicle facilities all have lower risk of infection. Similarly, a Danish study found that washing feet in 0.4% soap was beneficial for disease control (Thomsen et al., 2012). Many farmers have used the final rinse of parlor washings (containing sodium hypochlorite), although digital dermatitis epidemics have been triggered from contaminated baths as well (Bell and Main, 2011). Baths containing soap, parlor washings, or 2% hypochlorite could be useful for cleaning feet if used in alternation with other effective biocides. The physical hosing of feet can achieve the same effect, albeit with some increase in cow dunging behavior until the cows are accustomed to the practice.

Disinfectants

Best infection control is usually achieved when foot cleaning is combined with disinfection to remove any pathogens. There are a number of disinfectants that are used and have been reported (Bell et al., 2014), but only some of these are licensed under the EU Biocides Regulation 528/2012 (Table 2.2). The list of licensed biocides changes according to

Table 2.2. List of commonly used foot disinfection products for the control of digital dermatitis

Biocide	Usual footbath concentration	PT3 licence	Guidance for using footbaths[1]
Formalin (37% formaldehyde)	3–4% daily 2–2.5% in robotic systems 4–5% two to three times per week	Yes	Probable (class 1b) carcinogen and so can only be used by a competent (trained) person and appropriate personal protective equipment must be worn. Due to risk of formalin burns, it is unsafe to use frequently at more than 5% (unless under expert advice), especially in warm, windy (drying) conditions. Occasionally formaldehyde solution is sold in concentrations other than the standard 37%. Formalin should be stored according to the manufacturer's instructions. Formalin has a freezing point of -15°C, but formalin produced by the 'cold crack' method may have a higher freezing point.
Glutaraldehyde	2%	Yes	Not very effective in one topical treatment trial (Manske et al., 2002a). Toxic but probably not carcinogenic. More expensive than formalin. Personal protective equipment required for use.
Peracetic, lactic, and formic acid	1–5%	Yes	Can erode some types of concrete. Chemical burns can occur at high concentrations. Personal protective equipment required for use. Note that salicylic acid is a licensed biocide, but is not used in footbaths as far as we are aware.
Sodium hypochlorite	1–2%	Yes	Speijers et al. (2010) found that it was not any better than water when used weekly, but needs to be used daily and/or in rotation with another bathing product.
Soap	Follow label	Not a biocide	Cleans feet. Clean, dry skin with good condition is inherently more resistant to new infections (Thomsen et al., 2012).

The EU approve biocides as safe to use for veterinary hygiene purposes, listed on European Chemical Agency website within article 95, under category PT3.
[1]Read and adhere to Control of Substances Hazardous to Health (e.g., suitable personal protective equipment must be worn).

Table 2.2. (Continued). List of commonly used foot disinfection products for the control of digital dermatitis

Biocide	Usual footbath concentration	PT3 licence	Guidance for using footbaths[1]
Natural oils (e.g., teatree oil, Thymox; Laboratoire M2)	Follow label	Natural oils	Teatree oil is one component of Hoofsure Endurance (Provita). The authors have no experience of Thymox.
Crystalline copper sulphate	2–10% 1–2% when acidified to pH 3.5	No	Environmental hazard, toxic to sheep, and erodes galvanized metals. Commercial acidifiers are available (e.g., Healthy Hooves; Dengie, formalin, and pH Minus; Blue Horizons). Not an EU-approved biocide for animal use.
Zinc sulphate	10%	No	Heavy metal and a biohazard. It can be acidified like copper to reduce the required concentration. Should be used in crystalline form, not feed-grade zinc sulphate.
Commercial products and combinations	Follow label	Check	Check they contain licensed biocides and have published data supporting use.

The EU approve biocides as safe to use for veterinary hygiene purposes, listed on European Chemical Agency website within article 95, under category PT3.
[1]Read and adhere to Control of Substances Hazardous to Health (e.g., suitable personal protective equipment must be worn).

evidence regarding whether they pose an unacceptable risk to animals, people, or the environment. Furthermore, effective foot disinfection will prevent new infections, but it also appears to reduce the reactivation of M4 lesions and allows recovery of M1 and M4.1 lesions.

Formalin is one of the most commonly used footbath biocides (Stokes, 2011), and while it is currently approved under EU law, there has been discussion about its removal on the grounds that it is a probable carcinogen. Indeed, concerns over future litigation and general staff safety means that alternatives to formalin have been actively looked for.

Alternatives to Formalin

Given that treponemes do not survive in an environment with a pH 3 to 5, some advisers recommend the use of water acidifiers (e.g., sodium bisulphate) – these were originally adopted to ionise copper sulphate footbaths, but can be used alone. Glutaraldehyde is currently licensed and does not appear to have carcinogenic properties, but it is more expensive than formalin, has a similar toxicity, and appears to lack efficacy at recommended concentrations.

There are a number of commercial alternatives available, most without published efficacy data. The organic acids appear to be the most promising (e.g., peracetic acid and formic acid). Given that the low pH may be an important aspect to the biocidal nature of organic acids, some form of pH checks may be useful for monitoring footbath efficacy. All acids will also erode concrete and therefore acid-resistant concrete or alternative footbath construction materials are advisable.

Automated Systems

Given the potential human health and safety risks associated with handling the footbath biocides, automated footbathing systems are highly recommended. Like all automatic systems, they need to be closely monitored to ensure they are filling, dosing, emptying, and cleaning correctly. Dosing mistakes are extremely common in all systems (Holzhauer et al., 2004).

Chapter 2

Footbath Design

A novel footbath design has been proposed by a group of researchers from Wisconsin. The design maximizes the number of foot plunges for a given volume of footbath (Figure 2.4; Cook et al., 2012). This concept improves the washing and cleaning effect (more plunges), increases contact time with the biocide (longer time walking in the solution), and minimizes the volume, and therefore also the cost, of the solutions used.

Other experts in the field advocate 'double cow' width baths (or two in parallel) to maximize cow flow and minimize stress behavior. The use of two footbaths in series (i.e., including a 'pre-wash') reduces the contamination rate in the second treatment bath, although we advocate the use of biocide in both baths to maximize disinfecting opportunity. Alternatively, hosing feet clean in the parlor will also reduce contamination.

Standard recommendations for refreshing formalin baths are to replace the bath at a rate of one cow pass per litre of footbath solution (Holzhauer et al., 2004). Compartmentalized baths may become more important as more expensive biocides come into use to extend biocidal activity for more cow passes.

Figure 2.4. Wisconsin footbath design. Note the 28 cm high kerb which encourages more frequent, shortened steps for added plunges, as well as reducing solution loss (i.e., kickout). The solid sides promote better cow flow while again reducing solution loss. The 60 cm wide footwell is just wide enough to allow cows to walk comfortably, but allows for the length of bath to be extended to 3.7 to 4 m without inflating the volume excessively. The footbath is set at the existing floor level so the cow can step in and out with confidence.

One of the most important design features for any footbath is to make it easy to fill and easy to clean, so it is simple to use regularly. Indeed, foot disinfection should continue throughout the summer grazing period, as cattle can acquire new infections at any time of year.

Most footbathing protocols focus on the lactating groups which are easiest to footbath, but often the new infections arise in youngstock and dry cows which are often overlooked. Given that most infected animals remain bacteriologically infected for life, even following clinical resolution, efforts to prevent new infections in all management groups, (particularly youngstock) are worthwhile.

In general, footbathing two to three times per week with 4 to 5% formalin seems to maintain an acceptable level of infection control. This protocol should then progress towards the lowest footbathing frequency using the lowest product concentration that keeps the digital dermatitis status of the herd under control.

SUMMARY

Digital dermatitis is a highly contagious disease which responds well to a range of topical, licensed treatments and the rate of new infections can be easily controlled with regular foot disinfection. All stages of infection benefit from treatment, and with a concerted effort to reduce the reservoir of infection in animals, infection pressure can be reduced.

Latest concepts in digital dermatitis treatment are focused on treating digital dermatitis as an infected wound. New technologies could make the cleaning and disinfection of feet more practical and effective, to maximize the contact time between a clean foot and an effective biocide. Moreover, plunging a foot in biocide appears to be important for cleaning and disinfecting the pocket between the heel bulbs, meaning automated spray systems could result in disappointing outcomes.

The immediate challenge is to make daily foot cleaning and disinfection as simple, practical, and safe as possible for cows and farm staff, while optimizing the detection of infected cows for treatment. Ultimately, ensuring the foot is managed in a clean and dry environment with healthy skin may reduce the dependence on treatment and footbathing for many herds. Future advances are likely to focus on the genetic selection of cows that are resistant to new infections using genomics, in turn reducing the dependence on other control measures.

Chapter 2

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All will be pleased to know that we still disagree on some concepts but without loss of respect and admiration. Finally, we would like to thank the ICAR team for providing greater clarity on digital dermatitis lesion scoring.

COMPETING INTERESTS

No conflicts of interest arose in writing this article.

FURTHER RESOURCES

Approved biocides for skin disinfection, as listed under a category PT3 licence: https://echa.europa.eu/information-onchemicals/active-substance-suppliers (accessed 23 November 2020)

Advice for dairy producers, trimmers, vets, and consultants working to improve the feet of dairy cows: www.cattle-lameness.org.uk

Chapter 3

Photograph M-score Interobserver Agreement

Vanhoudt, A., D.A. Yang, T. Armstrong, J.N. Huxley, R.A. Laven, A.D. Manning, R.F. Newsome, M. Nielen, T. van Werven, and N.J. Bell. (2019) Interobserver agreement of digital dermatitis M-scores for photographs of the hind feet of standing dairy cattle. J. Dairy Sci. 102:5466–5474. doi:10.3168/jds.2018-15644.

ABSTRACT

Digital dermatitis is the leading infectious cause of lameness in dairy cattle and it affects their welfare and productivity worldwide. At the herd level, digital dermatitis is often assessed while cows are standing in a milking parlor and lesions are most commonly evaluated using the M-score. The objective of this study was to examine the interobserver agreement for M-scores of the feet of standing cattle, based on digital color photographs of dairy cattle hind feet. A total of 88 photographs and written descriptors of the M-score were sent to 11 scorers working at 10 different institutions in five countries. The scorers received no formal training immediately before scoring the photographs; however, all regularly used the M-score to score digital dermatitis. The answers for 36 photographs were excluded from the analysis because the photograph either had more than one M-stage as mode or not all scorers assigned an M-score to it. The M-scores of the 11 scorers from 52 photographs were available for analysis. Interobserver agreement was tested using Gwet's agreement coefficient (AC1) and the mode was assumed correct. Overall, moderate agreement emerged for the M-score (AC1 = 0.48). For the individual M-stages, almost perfect agreement existed for M0 (AC1 = 0.99), M1 (AC1 = 0.92), and M3 (AC1 = 0.82), and substantial agreement for M2 (AC1 = 0.61), M4 (AC1 = 0.65), and M4.1 (AC1 = 0.71). This outcome indicates the degree of individual variation in M-scoring in this context by unstandardized, experienced European observers, particularly for the M2-, M4-, and M4.1-stages. Standardized training is likely to improve the consistency of M-scoring and thus the generalizability of future digital dermatitis research results on this important endemic disease.

Key words: dairy cow, digital dermatitis, lameness, M-score, interobserver agreement

INTRODUCTION

Bovine digital dermatitis is an endemic infectious disease among farmed cattle. The characteristic active lesion of digital dermatitis is a painful, large, red to gray ulceration of the skin between the heel bulbs, with the hind feet most often affected. The chronic stage of digital dermatitis is a dyskeratotic or irregular proliferative hyperkeratotic dermatitis. Despite treatment and control measures, chronic stages often recrudesce into active stages, contributing to further infectious spread of digital dermatitis and resulting in lameness that compromises animal welfare and productivity (Willshire and Bell, 2009; Bruijnis et al., 2010, 2012a).

Several classification systems have been proposed to recognize and grade the visual characteristics of digital dermatitis lesions. Briefly, Döpfer et al. (1997) classified digital dermatitis lesions according to morphological observations [M-score, which was later adapted by Berry et al. (2012)]; Laven and Proven (2000) classified digital dermatitis lesions according to lesion color among other clinical signs; Manske et al. (2002a) classified digital dermatitis lesions according to severity and stage of development; Vink et al. (2009) classified digital dermatitis lesions according to size, clinical presentation, and location; and Krull et al. (2014) classified digital dermatitis lesions according to morphological appearance (Iowa-score). Following classification using the M-score, digital dermatitis lesions were grouped according to disease status as early, infectious, or healing by Döpfer et al. (2012) and as active or inactive by Zinicola et al. (2015b) and Biemans et al. (2018).

Recognition and grading of digital dermatitis lesions serves three purposes: (1) to study the pathophysiology of digital dermatitis (Rasmussen et al., 2012; Zinicola et al., 2015b; Nielsen et al., 2016), (2) to identify animals that need treatment (Schultz and Capion, 2013; Dotinga et al., 2017), and (3) to study the infection dynamics of digital dermatitis at a population level (Döpfer et al., 2012; Tremblay et al., 2016; Biemans et al., 2018). Currently, the M-score remains the most widely used, researched, and cited method. Although M-scoring cattle in the trimming chute is considered best practice, regular and repeated screening of herds for digital dermatitis commonly occurs during a pen walk or milking. Several studies have looked at the diagnostic test characteristics of scoring digital dermatitis lesions in the milking parlor using various digital dermatitis lesion classification systems and observations in the trimming chute as the gold standard. For digital dermatitis lesion classification systems other than the M-score, sensitivity ranges from 65 to 72% and specificity from 84 to 99% (Rodriguez-Lainz et al., 1998; Thomsen et al., 2008). Yang et al. (2017b) estimated a sensitivity of around 63% and specificity of nearly 100% for visual inspection of the rear feet for presence or absence of lesions of digital dermatitis during milking. M-scoring in the milking parlor, whether assisted by a telescopic mirror or not, appears to be both sensitive (90 to 100%) and specific (80 to 99%) in identifying cattle with digital dermatitis (Relun et al., 2011; Stokes et al., 2012a; Solano et al., 2017a), although some misclassification has been reported when compared with M-scoring in the trimming chute, especially for M3 (Relun et al., 2011) and M4.1 (Solano et al., 2017a). More recently, Cramer et al. (2018) reported a sensitivity of around 58% and specificity of around 95% after dichotomizing the M-score.

Although the M-score is used by researchers, foot trimmers, farmers, and veterinarians, the methods by which scorers are trained are rarely mentioned in the published literature. In some publications, “an experienced or trained scorer” produces M-scores (Logue et al., 2012; Higginson Cutler et al., 2013; Kulow et al., 2017), whereas elsewhere scorers undergo a detailed training program consisting of recognizing M-stages from color photographs, sometimes followed by scoring live animals (Alsaaod et al., 2014; Solano et al., 2017a; Yang et al., 2017a). In the absence of standardized training programs, the reliability and repeatability of digital dermatitis scoring depends heavily on accurate and consistent interpretation of detailed lesion descriptors written in English. Yet to date, as far as we are aware, the interobserver agreement on M-scoring among scorers working in different institutions has not been studied.

The aim of this study was to assess interobserver agreement of the M-score based on photographs of standing animals. Using several agreement analyses, we calculated the interobserver agreement of the M-score (Döpfer et al., 1997; Berry et al., 2012) among unstandardized, experienced scorers working in different institutions, using single digital color photographs of the hind feet of standing dairy cattle.

MATERIALS AND METHODS

Scorers and Photographs

A convenience sample of 88 digital color photographs of the hind feet (plantar view) of standing dairy cattle was compiled from the personal libraries of four scorers (all from the UK), who respectively contributed 60, 17, eight, and three photographs. The photographers were asked to provide photographs from their libraries with high image quality (in focus and taken in a well-lit environment) and absence of lesions other than digital dermatitis and to include photographs of feet without digital dermatitis. All but one photograph were marked with ownership. Four photographs were assisted with a telescopic mirror. Nine photographs were annotated with "raised" and one with "raised/thickened" features important for scoring that could be seen in real life, but might not be apparent on a photograph. The light source in the photographs varied between natural and artificial light sources, including a headlamp. Photographs were taken at varying angles to and distances from the hind feet (estimated range 10 to 50 cm). The photographed feet were of varying cleanliness. A survey containing the photographs was created in Google forms (Google LLC). The resolution of the original photographs ranged from 1,600 × 1,200 to 3,264 × 1,836 pixels. For compatibility with the Google forms survey, the photographs had to be compressed to resolutions ranging from 269 × 293 to 740 × 991 pixels. An email with the modified M-score descriptors (Table 3.1; Döpfer et al., 1997; Berry et al., 2012) and a URL (http://bit.ly/M-score_survey) to the survey was sent to 11 scorers, all of whom had scored digital dermatitis regularly in the past using the M-score. The scorers were asked to complete the survey as they would normally M-score cattle when out on farms. The survey needed to be completed before a certain date, but the time spent on it was not otherwise restricted. The 11 scorers were a convenience sample, without sample size calculation, from within the personal network of the principal investigator. The principal investigator selected the scorers based on them having at least met the proficiency level of the five-stage model of adult skill acquisition of clinical skills (Dreyfus, 2004). The scorers received no formal training or standardization immediately before the exercise. Scorers could also choose "Don't know" or write a comment for

Table 3.1. M-score: M-stage and descriptors, as provided to the scorers

M-stage[1]	Descriptor
M0 or M5[2]	No sign of preexisting lesion. Normal skin.
M1	Small (<2 cm across) focal active state. Circumscribed lesion. Surface is moist, ragged, mottled red–gray with scattered small (~1 mm diameter) red foci.
M2	Larger (>2 cm across) ulcerative active stage. Extensively mottled red–gray. Can be painful upon manipulation.
M3	Healing stage. Typically seen within a few days after antibiotic treatment. The ulcerated surface is now transformed to a dry brown, firm rubbery scab. No pain on manipulation.
M4	Chronic stage. Surface is raised by tan, brown, black, rubbery, irregular, proliferative hyperkeratotic growths that vary from papilliform to mass-like projections.
M4.1	Chronic stage with small active painful M1 focus.

[1]As described by Döpfer et al. (1997) and adapted by Berry et al. (2012).
[2]The M0-stage is more commonly used than the M5-stage described by Berry et al. (2012).

each photograph. Scorers provided the M-scores without interobserver consultation. Upon completion of the survey, scorers gave permission to use their data for this research. All 11 scorers answered the survey.

Statistical Analysis

Data were collected by means of Google forms and collated into a spreadsheet (MS Excel). Although M-scores were reported for all photographs, statistical analysis excluded photographs with more than one M-stage as mode and photographs not M-scored by all scorers. For each photograph, the mode was assumed the correct M-score.

First, the overall mean percentage raw agreements with the mode (**PA_o**; number of exact agreements / total number of observations × 100,) with 95% confidence interval and mean PA_o with 95% confidence interval for each M-stage were calculated. Because the PA_o did not consider the interobserver agreement to be due to chance, we calculated overall Fleiss's kappa (**κ**) with 95% confidence interval (Fleiss, 1971), as well as κ with 95% confidence interval for each M-stage individually. By comparing the PA_o and κ for the individual M-stages, we found a paradox: some M-stages had a high PA_o with a low κ. Therefore, a baseline-category logit model using M-stage as the outcome variable and scorer as a predictor was fitted and the predicted probabilities of reporting each M-stage (category) by each scorer were calculated as follows. Let Y be a nominal outcome with J categories ($J = 1, 2, 3, \ldots, j$) with the probability $\pi_j(X) = P(Y = j|X)$ at a fixed X (the predictor); therefore, $\Sigma_j \pi_j(X) = 1$. Each category J for the outcome Y had probabilities $\{\pi_1(X), \pi_2(X), \ldots, \pi_j(X)\}$. The model relating the probability of category j to that of a baseline category (for example, $J = 1$) could then be formulated as

$$\ln\left(\frac{\pi_j(X)}{\pi_1(X)}\right) = \beta_0^{(j)} + \beta_1^{(j)}X,$$

where β_0 is the intercept and β_1 measures the effect of scorers for each of the J categories. The predicted probability for any scorer reporting any category was

$$\pi_j(X) = \frac{e^{\beta_0^{(j)} + \beta_1^{(j)}X}}{1 + \sum_{j=1}^{J} e^{\beta_0^{(j)} + \beta_1^{(j)}X}}.$$

The variances (**σ^2**) of the predicted probabilities for each M-stage were used as indicators to describe the variability across scorers for each M-stage. This approach revealed that the high PA_o together with a low κ for some M-stages was due to unequal prevalence (based on the mode) of the M-stages in our data set. Finally, for more robust and relevant measurement of interobserver agreement, Gwet's agreement coefficient (**AC1**; Gwet, 2008) was used as it is less sensitive to either marginal homogeneity or trait prevalence. Gwet's AC1 with 95% confidence interval was calculated for overall agreement and each M-stage separately. We recalculated Gwet's AC1 with 95% confidence interval for overall agreement after condensing several M-stages into different groups (Table 3.2).

The analysis of the baseline-category logit model was done using Stata 13.1 (StataCorp LLC), and all other statistical analyses were done using R (R Core Team, 2014). For all measures of agreement, the guidance provided by Landis and Koch (1977) for the interpretation of κ was used: <0.00, poor; 0.00 to 0.20, slight; 0.21 to 0.40, fair; 0.41 to 0.60, moderate; 0.61 to 0.80, substantial; and 0.81 to 1.00, almost perfect.

Table 3.2. Overview of the groups of M-stages used for Gwet's agreement coefficient (AC1) calculation

	M-stage[1]					
Grouping criterion	M0[2]	M1	M2	M3	M4	M4.1
Lesion color (Laven and Proven, 2000)	No lesion	Red	Red	Black	Gray	Gray
Infectious disease modeling by Döpfer et al. (2012)	No lesion	Early	Infectious	Healing	Infectious	Infectious
Infectious disease modeling by Biemans et al. (2018)	No lesion	Active	Active	Inactive	Inactive	Active
Absence or presence of digital dermatitis	No lesion	Lesion	Lesion	Lesion	Lesion	Lesion

[1]As described by Döpfer et al. (1997) and adapted by Berry et al. (2012).
[2]The M0-stage is more commonly used than the M5-stage described by Berry et al. (2012).

RESULTS

Scorers and Photographs

The 11 scorers were geographically distributed over England (7), the Netherlands (1), Northern Ireland (1), the Republic of Ireland (1), and Spain (1). Six scorers were employed by five different universities, two by different agricultural companies, and three were self-employed veterinary consultants. Ten scorers held a degree in veterinary medicine and one scorer in agri-food and business studies. Most of the scorers (9) also held at least one postgraduate degree. At the moment of answering the survey, two scorers were senior researchers in the field of bovine lameness; two scorers had recently obtained a PhD in a relevant field; two scorers were PhD candidates in a relevant field; two scorers were residents of the European College of Bovine Health Management; two scorers were in a commercial role, with one having obtained a PhD on digital dermatitis; and one scorer was a farm animal veterinary consultant. Between the scorers, experience in using the M-score varied, with six scorers having one to five years of experience, four scorers having six to 10 years of experience, and one scorer having 16 to 20 years of experience.

All but one scorer assessed all the photographs. One scorer could not assess three photographs due to an error in opening them and one photograph received a blank response from this scorer. Another scorer gave the general comment "The diagnosis of M1 and M3 is limited from pictures as M1 is difficult to spot and M3s by definition occur as a transitory state after treatment.". That scorer did not assign any photograph with the M1- or M3-stage. The number of photographs assigned an M-stage by each scorer ranged from 76 to 88, with four scorers assigning an M-stage to all 88 photographs. Table 3.3 summarizes the assigned M-scores and the modes for the 88 photographs. The answers for six (7%) photographs were excluded because they had more than one M-stage as mode (e.g., photograph 30 was scored as M3 by five scorers, M4 by five scorers, and M4.1 by one scorer) and the answers for 30 (34%) photographs were excluded because they did not receive an M-stage from all scorers (21 photographs were not given an M-stage by one scorer, three by two scorers, three by three scorers, and three by four scorers). The M-scores

Table 3.3. Descriptive data showing the M-scores[1] assigned to 88 digital color photographs of the hind feet of standing dairy cattle by 11 experienced but unstandardized scorers; the frequencies of "correct" (mode[2]; bold) and other classifications are shown, both for the number of M-scores assigned and the number of photographs that the scores were assigned to

	Actual classification, count of scores given (count of photographs)					
Item	M0[3]	M1	M2	M3	M4	M4.1
M0	**93 (10)**	3 (3)	1 (1)	1 (1)	5 (4)	0 (0)
M1	1 (1)	**18 (4)**	2 (2)	4 (3)	7 (3)	3 (2)
M2	0 (0)	14 (8)	**158 (22)**	13 (6)	11 (6)	42 (19)
M3	2 (1)	18 (9)	8 (6)	**57 (14)**	52 (14)	3 (3)
M4	6 (3)	28 (15)	25 (13)	100 (42)	**277 (45)**	27 (17)
M4.1	0 (0)	1 (1)	20 (7)	7 (4)	11 (5)	**48 (8)**

[1]As described by Döpfer et al. (1997) and adapted by Berry et al. (2012).
[2]The mode (bold type) was taken to be the correct classification. For 11 photographs, there were two modes, and for two photographs, there were three modes.
[3]The M0-stage is more commonly used than the M5-stage described by Berry et al. (2012).

for 52 (59%) photographs were used for analysis. The resolution after compression for the survey was 740 × 555 pixels for the six photographs excluded for having more than one M-stage as mode, ranged from 269 × 293 to 740 × 991 pixels for the 30 photographs excluded for not receiving an M-stage from all scorers, and ranged from 505 × 367 to 740 × 991 pixels for the 52 photographs used for analysis.

Agreement Analyses

At the level of the scorer, mean PA_o (95% CI) was 72% (64 to 79%) and mean PA_o at the level of the photograph was also 72% (67 to 76%). We found 100% agreement for only five (10%) photographs (four M0 and one M4) and at least 60% agreement for 40 (77%) photographs. For each M-stage and overall for the M-score, the results of the statistical agreement analyses (i.e., PA_o, κ, σ^2, and AC1) are given in Table 3.4. After grouping the M-stages, the overall AC1 (95% CI) for the M-score was 0.56 (0.49 to 0.64, $P < 0.001$) for lesion color as used by Laven and Proven (2002), 0.74 (0.67 to 0.81, $P < 0.001$) for infectious disease modeling classification as used by Döpfer et al. (2012), 0.78 (0.71 to 0.86, $P < 0.001$) for infectious disease modeling classification as used by Biemans et al. (2018), and 0.99 (0.98 to 1.00, $P < 0.001$) for absence or presence of a digital dermatitis lesion.

Table 3.4. Statistical analyses for agreement with the mode with 95% confidence interval (CI) for each M-stage[1] and overall for the M-score[1] from 52 digital color photographs of the hind feet of standing dairy cattle assessed by 11 experienced but unstandardized scorers

Variable	Overall	M0[2]	M1	M2	M3	M4	M4.1
N[3]	52	6	1	19	1	19	6
Percent raw agreement (95% CI)	72 (67–76)	97 (94–100)	73[4]	68 (61–75)	55[4]	71 (64–77)	61 (51–71)
Fleiss's κ (95% CI)	0.44*** (0.36–0.53)	0.96*** (0.92–1.00)	0.23* (0.00–0.48)	0.45*** (0.35–0.56)	0.10** (0.02–0.18)	0.51*** (0.40–0.61)	0.23*** (0.12–0.34)
Variance[5]	—	0.000	0.003	0.013	0.005	0.007	0.014
Gwet's agreement coefficient, AC1 (95% CI)	0.48*** (0.41–0.56)	0.99*** (0.98–1.00)	0.92*** (0.88–0.97)	0.61*** (0.46–0.75)	0.82*** (0.74–0.89)	0.65*** (0.51–0.79)	0.71*** (0.61–0.82)

[1]As described by Döpfer et al. (1997) and adapted by Berry et al. (2012).
[2]The M0-stage is more commonly used than the M5-stage described by Berry et al. (2012).
[3]Number of photographs (with this M-stage as the mode).
[4]No 95% confidence interval for the mean percentage raw agreement with the mode for single observations.
[5]Variances of the predicted probabilities of reporting each M-stage by each scorer following baseline-category logit model analysis.
*P = 0.08, **P = 0.01, ***P < 0.001 (within rows).

DISCUSSION

This study demonstrates the variation in agreement between users when M-scoring digital color photographs of the hind feet of standing dairy cattle. Overall, mean PA_o was around 70% at the level of the photograph. The PA_o between observers for the individual M-stages was moderate (M3), substantial (M1, M2, M4, and M4.1), or almost perfect (M0). Fleiss's κ analysis highlights that agreement is poorer when adjusted for agreement due to chance (slight for M3, fair for M1 and M4.1, moderate for M2 and M4, and almost perfect for M0). Using Gwet's AC1, which accounts for marginal homogeneity and trait prevalence, we found an improvement in the interobserver agreement for all M-stages when compared with κ agreement (substantial for M2, M4, and M4.1, and almost perfect for M0, M1, and M3). The overall AC1 agreement for the M-score improved in comparison with overall κ agreement (κ = 0.44), but remained only moderate (AC1 = 0.48).

Few studies have looked at interobserver agreement of the M-score (Relun et al., 2011; Solano et al., 2017a; Biemans et al., 2018) and of these, only one describes the interobserver agreement of the M-score when applied to digital color photographs of hind feet (Solano et al., 2017a) (Table 3.5). In these studies, Cohen's κ is used to measure interobserver agreement (Cohen, 1960). This study is the first using Fleiss's κ and Gwet's AC1 to investigate interobserver agreement of the M-score when applied to digital color photographs of hind feet, thereby accounting for having more than two observers, marginal homogeneity, trait prevalence, and agreement due to chance with a more reasonable assumption. It is impossible to know what the interobserver agreement would have been in the other studies had they used Fleiss's κ, Gwet's AC1, or both, which impedes interpreting the results from this study in light of those from previous studies.

Care should be taken in comparing the interobserver agreement of the M-score from digital color photographs of cattle feet with those from studies using live animals. Digital color photographs show the feet in a set two-dimensional view (versus a changeable three-dimensional view in real life), which makes estimating the dimensions of the lesion difficult and thereby limits the observer's ability to interpret the presented foot. Also, certain aspects of the M-score descriptors cannot be considered when scoring from photographs (i.e., reaction on manipulation and treatment history). However, these difficulties apply equally to the screening of standing animals during pen walks or in the milking parlor. Further, treatment history is not clearly stated as an essential criterion in the M-score descriptors, and only one scorer commented that treatment history was unknown; this scorer consequently did not assign the M3-stage (or M1-stage) to any photograph. This scorer also did not assign an M-stage to four photographs. The mode for these four photographs was neither M1 nor M3. Because scorers did not explain why they did not assign an M-score to a photograph, the true reason for not assigning an M-score to any photograph is unknown. Future digital dermatitis research using photographs of cattle feet should alleviate the limitations of M-scoring photographs as much as possible by using novel image capture techniques to resemble human vision (e.g., stereo-vision capture systems) or including a ruler in the photograph and using photographs taken under standard conditions, that is, using the same camera under the same lighting conditions, and taken by the same photographer at the same distance and angle to the foot.

The advantages of M-scoring from photographs are that the animals do not move and there is no time pressure, unlike when M-scoring live animals during milking. It also allows more effective blinding of observers, thereby accounting for observer drift. Using photographs of cattle feet for digital dermatitis research offers the opportunity to amass scorers from a large population of researchers for international standardization, with guidance on interpretation from the most experienced and competent scorers or a remotely located expert scorer.

The level of interobserver agreement in our study is lower than that reported by others regardless of whether they scored digital color photographs or live animals. One possible reason for the lower interobserver agreement in this study is the lack of the prestudy training, which was provided in some other studies (Relun et al., 2011; Solano et al., 2017a; Biemans et al., 2018). As far as we are aware, this study is the first to assess the M-score interobserver agreement with observers from (10) different institutions. This factor may have contributed to the lower interobserver agreement in this study compared with previous studies using observers

Table 3.5. Overview of interobserver agreement statistics with 95% confidence interval (CI) for the M-score[1] from this study and those found in the published literature

Study objects and study	N scorers	M-score[1]	Experimental units	Interobserver agreement statistic (95% CI)		
				Percent raw agreement[2]	Kappa	Gwet's agreement coefficient[3]
Photographs						
This study	11	6-Stage	52 digital color photographs of hind feet taken from standing dairy cattle (plantar view)	72 (67–76)	Fleiss[4]: 0.41 (0.33–0.49)	0.48 (0.41-0.56)
Solano et al. (2017a)	3	6-Stage	40 digital color photographs of hind feet (start study)	83 (70–94)	Cohen[5]: 0.77 (0.67–0.86)	—
			40 digital color photographs of hind feet (midway study)	88 (76–98)	Cohen: 0.83 (0.74–0.90)	—

[1]As described by Döpfer et al. (1997) and adapted by Berry et al. (2012); the M0-stage is more commonly used than the M5-stage described by Berry et al. (2012); 5-stage classification (M0, M1, M2, M3, and M4) or 6-stage classification (M0, M1, M2, M3, M4, and M4.1).
[2]Percent raw agreement is the number of exact agreements divided by the total number of observations multiplied by 100.
[3]Gwet's agreement coefficient is suitable for multiclass, multi-observer interobserver agreement analysis. It corrects for agreement due to chance with a more reasonable assumption and thus is less sensitive to either marginal homogeneity or trait prevalence (Gwet, 2008).
[4]Fleiss's kappa is suitable for multiclass, multi-observer interobserver agreement analysis and corrects for agreement due to chance (Fleiss, 1971).
[5]Cohen's kappa is suitable for multiclass interobserver agreement analysis of two observers and corrects for agreement due to chance (Cohen, 1960).

Table 3.5 (Continued). Overview of interobserver agreement statistics with 95% confidence interval (CI) for the M-score[1] from this study and those found in the published literature

				Interobserver agreement statistic (95% CI)		
Study objects and study	N scorers	M-score[1]	Experimental units	Percent raw agreement[2]	Kappa	Gwet's agreement coefficient[3]
Live animals						
Relun et al. (2011)	5	5-Stage	Hind feet from 242 cows in the milking parlor	66 (62–70)	Cohen[4]: 0.51 (0.45–0.56)	—
Solano et al. (2017a)	3	6-Stage	Hind feet from 110 cows in the milking parlor	82 (73–90)	Cohen: 0.74 (0.69–0.78)	—
Biemans et al. (2018)	2	6-Stage	204 hind feet in the milking parlor (start study)	—	Cohen: 0.75 (0.66–0.84)	—
			164 hind feet in the milking parlor (during study)	—	Cohen: 0.85 (0.78–0.93)	—
			52 hind feet in the milking parlor (during study)	—	Cohen: 0.76 (0.61–0.90)	—

[1]As described by Döpfer et al. (1997) and adapted by Berry et al. (2012); the M0-stage is more commonly used than the M5-stage described by Berry et al. (2012); 5-stage classification (M0, M1, M2, M3, and M4) or 6-stage classification (M0, M1, M2, M3, M4, and M4.1).
[2]Percent raw agreement is the number of exact agreements divided by the total number of observations multiplied by 100.
[3]Gwet's agreement coefficient is suitable for multiclass, multi-observer interobserver agreement analysis. It corrects for agreement due to chance with a more reasonable assumption and thus is less sensitive to either marginal homogeneity or trait prevalence (Gwet, 2008).
[4]Cohen's kappa is suitable for multiclass interobserver agreement analysis of two observers and corrects for agreement due to chance (Cohen, 1960).

working in the same institution (Relun et al., 2011; Solano et al., 2017a; Biemans et al., 2018). Future research is needed to confirm this possibility. Because the diversity of the scorers in our study may have contributed to the difference in interobserver agreement, it may also cast doubt over the comparability of international digital dermatitis research. It is possible that scorer characteristics, such as sex, age, type of qualification, years of experience in applying the M-score, and the method of training in digital dermatitis scoring, could influence interobserver agreement. Unfortunately, these influences could not be investigated in our study.

We did find that grouping the M-stages resulted in higher AC1 agreements. Grouping certain M-stages, as both Relun et al. (2011) and Solano et al. (2017a) found, yields higher interobserver agreement. In this study, dichotomizing the M-score as absent or present resulted in the highest overall AC1 interobserver agreement (0.99). This is also reflected in the almost perfect agreement between the scorers for the photographs with M0 as the mode in this study, regardless of the type of statistical agreement analysis. We interpret this finding as implying that all scorers are generally well able to identify cattle with and without digital dermatitis on digital color photographs of the hind feet of standing dairy cattle. Further research is needed to identify which M-stages should be grouped for each type of use (pathophysiology, treatment, or infection dynamics of digital dermatitis) and scorer (researcher, foot trimmer, farmer, or veterinarian) to enable highest interobserver agreement, while maintaining sufficient diagnostic test characteristics such as sensitivity and specificity.

In our data set, 30 photographs were not assigned an M-stage by every scorer, meaning that at least one scorer was unsure which M-stage the photograph represented. This was likely to be a consequence of lesion descriptor interpretation, photograph limitations (versus real life), lesion complexity, the standing position of the leg (versus inspecting raised feet in the trimming chute), or a combination of these factors. Unfortunately, during data collection scorers were not asked to give their reason for not assigning an M-stage to a photograph. Excluding these 30 photographs and the six photographs with more than one M-stage as the mode likely caused a bias toward the best quality photographs because all scorers were presumably confident about their M-scores for the remaining 52 photographs that were used for agreement analysis.

Achieving high interobserver agreement for the recognition and classification of digital dermatitis lesions is crucial for international generalizability and applicability of the results from digital dermatitis research. The development of an internationally available digital dermatitis training program would likely help in achieving high interobserver agreement for the recognition and classification of digital dermatitis lesions, although this outcome should be confirmed in future research. Any future digital dermatitis training program should take into account the intended use of the classification system (pathophysiology, treatment, or infection dynamics of digital dermatitis) and user type (researcher, foot trimmer, farmer, or veterinarian). In addition, the application of automated digital dermatitis lesion recognition and classification using novel image capturing techniques and artificial intelligence should be researched and developed. This approach would enable early cow-side diagnosis of cattle eligible for treatment and disease status monitoring, both on farms with automated milking systems and on farms with conventional milking systems.

CONCLUSIONS

The aim of this study was to investigate the interobserver agreement of the M-score applied to digital color photographs of the hind feet of standing dairy cattle when scored by observers working in different institutions. We studied the external validity of the M-score, which reflects the generalizability of the results from digital dermatitis research using the M-score. The results from this study indicate that the external validity of the M-score is almost perfect when dichotomized as the absence or presence of a digital dermatitis lesion but lower for the M2-, M4-, and M4.1-stages, the three stages that are assigned important roles in the clinical aspect or epidemiology of digital dermatitis. Achieving high interobserver agreement for all the M-stages between scorers globally would greatly benefit the investigation of digital dermatitis because it will contribute to the comparability of future digital dermatitis research results. We propose that standardized training of scorers would likely improve the consistency between scorers, and this possibility should be the focus of future research.

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COMPETING INTERESTS

No conflicts of interest arose in writing this article.

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Chapter 4

Infrared Thermography for Digital Dermatitis Detection

Vanhoudt, A., C. Jacobs, M. Caron, H.W. Barkema, M. Nielen, T. van Werven, and K. Orsel. (2023) Broad-spectrum infrared thermography for detection of M2 digital dermatitis lesions on hind feet of standing dairy cattle. PLoS One 18:1–14. doi:10.1371/journal.pone.0280098.

ABSTRACT

Low-effort, reliable diagnostics of digital dermatitis are needed, especially for lesions warranting treatment, regardless of milking system or hygienic condition of the feet. The primary aim of this study was to test the association of infrared thermography from unwashed hind feet with painful M2 lesions under farm conditions, with lesion detection as ultimate goal. Secondary objectives were to determine the association between infrared thermography from washed feet and M2 lesions, and between infrared thermography from unwashed and washed feet and the presence of any digital dermatitis lesion. A total of 641 hind feet were given an M-score and infrared thermography images of the plantar pastern were captured. Multivariable logistic regression analyses were done with digital dermatitis status as dependent variable and maximum infrared temperature (IRTmax), lower leg cleanliness score, and locomotion score as independent variables, and farm as fixed effect. To further our understanding of IRTmax within digital dermatitis status, we divided IRTmax into two groups over the median value of IRTmax in the datasets of unwashed and washed feet, respectively, and repeated the multivariable logistic regression analyses. Higher IRTmax from unwashed hind feet were associated with M2 lesions or digital dermatitis lesions, in comparison with feet without an M2 lesion or without digital dermatitis, adjusted odds ratio 1.6 (95% CI 1.2 to 2.2) and 1.1 (95% CI 1.1 to 1.2), respectively. Washing of the feet resulted in similar associations. Dichotomization of IRTmax substantially enlarged the 95% confidence interval for the association with feet with M2 lesions indicating that the association becomes less reliable. This makes it unlikely that IRTmax alone can be used for automated detection of feet with an M2 lesion. However, IRTmax can have a role in identifying feet at-risk for compromised foot health that need further examination and could therefore function as a tool aiding in the automated monitoring of foot health on dairy herds.

INTRODUCTION

Digital dermatitis is a multifactorial, infectious, polytreponemal disease, characterized by ulcerative or hyperkeratotic lesions that are typically located between the heel bulbs of hind feet (Orsel et al., 2018). It affects dairy cattle worldwide and cattle with digital dermatitis have reduced animal welfare, production, and reproductive performance, resulting in economic losses and increased labor for the farmers (Bruijnis et al., 2012a; Higginson Cutler et al., 2013; Dolecheck and Bewley, 2018).

Current control of digital dermatitis relies on keeping the disease in a manageable state (Döpfer and Bonino Morlán, 2008) and entails both disease prevention through footbathing at herd level and treatment of ulcerative lesions at cow level. These ulcerative lesions are commonly grouped as active lesions and consist of the M1-, M2-, and M4.1-stage lesions (Zinicola et al., 2015b).

Detection of digital dermatitis lesions is often late and typically takes place either during routine foot trimming or when cows are seen lame or standing on tiptoes due to a painful lesion. Visual inspection of the feet in the trimming chute is considered best practice for the diagnosis of digital dermatitis (Solano et al., 2017a). However, often this is not practical due to time and labor requirements and typically is not performed on a routine basis at herd level, which is essential for early detection and treatment of M2 lesions (Cramer et al., 2018). Prompt effective treatment of M2 lesions deals with the welfare aspect of digital dermatitis, as Higginson Cutler et al. (2013) described these lesions as most painful.

Consequently, scoring feet in the milking parlor after feet have been hosed off with water was successfully tested as an alternate diagnostic tool, compared to identification in the trimming chute, with a sensitivity and specificity for detecting M2 lesions of about 0.60 and 1.00, respectively (Solano et al., 2017a). Others compared scoring in the milking parlor with the trimming chute for presence or absence of a digital dermatitis lesion, regardless the M-stage, and reported sensitivities ranging from 0.55 to 1.00 and specificities ranging from 0.80 to 1.00 (Relun et al., 2011; Stokes et al., 2012a; Cramer et al., 2018). Due to the absence of a milking parlor on dairy herds with an automatic milking system, routine screening of digital dermatitis on these herds must occur during pen walks or by running the entire herd through the trimming chute. Cramer et al. (2018) reported pen walks to have poor discerning capacity for M-stages of digital dermatitis.

There is, therefore, an urgent need for a reliable method to quickly and easily diagnose M2 lesions which is widely applicable regardless the hygienic condition of the feet, nor dependent of milking system. A small number of studies investigated the use of infrared thermography for the purpose of detecting the presence of digital dermatitis, regardless the M-stage. This technology is based on detecting infrared radiation, which is emitted by all objects, depending on their temperature. Skin temperature is highly dependent on the temperature of the underlying tissue and circulation. Therefore, variations in skin temperature, captured by an infrared thermography camera, can be related to underlying inflamed tissue or altered metabolic activity (Mota-Rojas et al., 2021), as may occur during inflammation caused by digital dermatitis. In a study by Stokes et al. (2012b), maximum infrared temperature (**IRTmax**) of the plantar pastern was higher on feet with digital dermatitis from standing cattle in comparison with feet without any lesions. However, IRTmax was not different between feet with digital dermatitis lesions and feet with other lesions (Stokes et al., 2012b). Alsaaod et al. (2014) were able to detect hind feet with digital dermatitis in standing cows using the difference between IRTmax of hind and front feet.

For practical and technical reasons, M2 detection on unwashed feet is preferred over detection on pre-washed feet (Stokes et al., 2012b). The primary objective of this study was, therefore, to determine whether broad spectrum infrared thermography from unwashed hind feet of cows standing in a milking parlor was associated with M2 lesions. As secondary objectives, we investigated the association of infrared thermography from pre-washed standing hind feet with M2 lesions and the association of infrared thermography from unwashed and washed standing hind feet with the presence of digital dermatitis, regardless of M-score.

MATERIALS AND METHODS

Study Design and Ethical Statement

We analyzed data collected in parallel with the published randomized controlled trial by Jacobs et al. (2017b). The infrared thermography measurements and locomotion scores were not analyzed before, whereas the M-scores, lower leg cleanliness scores, and farm descriptives were used from Jacobs et al. (2017b). All methods were approved by the Animal Care Committee (AC13-0055) of the University of Calgary. Written informed consent was obtained from the herd owners prior to participation in the study.

Participating dairy farms met the following criteria: ≥60 lactating dairy cows, >90% Holstein-Friesian cows, lactating cows housed in freestall barns and milked in a parlor. On a convenience sample of four farms, a target of 40 dairy cows were semi-randomly selected by dividing the number of milking cows, as stated by the farmer, by 40 and selecting every n^{th} cow in the milking parlor. These four farms were visited at three-week intervals for a total of 12 weeks, resulting in five visits with data collection per farm. An opportunistically selected fifth farm, was visited once to collect infrared thermography images and M-scores only. On this fifth farm, data was collected from as many hind feet as possible without delaying the milking routine. This resulted in data collection from 131 of the 186 cows being milked during the visit. Each farm was located in Alberta, Canada, and data were collected from May to August 2013 on the first four farms and in November 2013 on the fifth farm. The routine treatment and hoof trimming schedule was maintained for all farms over the course of the study (Jacobs et al., 2017b). We refer the reader to Jacobs et al. (2017b) for details on the footbathing practices for lactating cows. Where farm 1 corresponds with farm C4, farm 2 with farm C3, farm 3 with Q3, farm 4 with Q4, and farm 5 with Q6 in Jacobs et al. (2017b).

Clinical Scores and Infrared Thermography Data Collection

One observer (CJ), trained in scoring using digital color images, videos, and definitions, scored all feet in the study and took all infrared thermography images. During data collection the observer was aided by one other person to keep records. All data were collected during milking from both standing hind feet of recruited cows only. First, data were collected from recruited cows on one side of the parlor, followed by recruited cows on the other side of the parlor. The order of data collection remained the same throughout the study: lower leg cleanliness score, infrared thermography image capture of unwashed feet, wash feet with water using a water source that was available in the parlor, infrared thermography image capture of washed feet, and M-score washed feet. For the infrared thermography images of washed feet, the amount of time between washing feet and capturing the infrared thermography image varied according to the milking routine and size of the milking parlor. Recruited cows were video recorded while exiting the milking parlor and these recordings were used for locomotion scoring.

The lower leg cleanliness score was done as developed by Cook (2006) and adapted by Solano et al. (2015) and was scored from 1 to 4 according to varying contamination: 1 = fresh manure for <50%; 2 = fresh manure for >50%; 3 = dried caked and fresh manure for >50%; and 4 = entire area with dried caked manure. Scoring for digital dermatitis was according to the M-stage classification developed by Döpfer et al. (1997), using a headlamp and a cosmetic mirror glued to a kitchen spatula (Relun et al., 2011; Solano et al., 2017a). In summary, M0 was defined as normal digital skin with no evidence of digital dermatitis; M1 was defined as a small (<2 cm in diameter) circumscribed red to gray epithelial defect; M2 was defined as an ulcerative lesion ≥2 cm in diameter with a red to gray surface; M3 was defined as a stage characterized by a firm dark scab-like covering; and M4 was characterized by a lesion surface with brown or black tissue that was hyperkeratotic, scaly, or proliferative. As in Jacobs et al. (2017b), the M4.1 lesions, with small red circumscribed lesions occurring within the boundaries of an existing M4 lesion (Berry et al., 2012), were not scored as such, and therefore lesions of this description were included within the M1 category. The locomotion score considered five classes, with 1 = perfect gait and 5 = severely lame, based on the seven specific gait attributes as described by Flower and Weary (2006) and validated for use on video recordings by Chapinal et al. (2009) and Ito et al. (2010).

Infrared Thermography Imaging

Thermal images of all hind feet enrolled in the study were obtained with a FLiR i3 handheld thermal imaging camera[2] (FLiR Systems Inc.) and analyzed using ThermaCAM Researcher Professional 2.8 SR-2 software (FLiR Systems Inc.). The software package produced specific information such as minimum, maximum, and mean temperature with standard deviation for whole images or within a specific area using a geometric figure drawn on the image. Thermal images of the plantar pastern, focused on the cleft between the heel bulbs, were taken at a distance of approximately 0.5 m. To analyze the infrared thermography images, the rectangle tool of the software was used to select the plantar aspect of the hind feet from the bottom of the dewclaws to the heel (Figure 4.1). The processing of all infrared thermography images in the software, including the drawing of the rectangles, was done by one observer (MC). Previous studies identified IRTmax as the most suitable infrared thermography variable for research on the association between infrared thermography and foot health (Stokes et al., 2012b; Harris-Bridge et al., 2018), hence we only used IRTmax for the

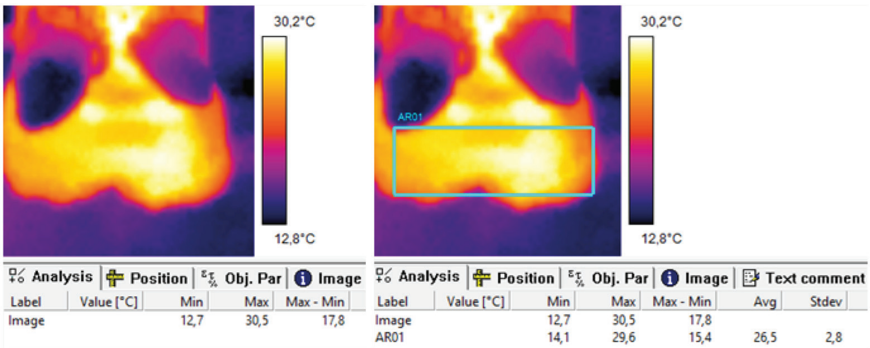

Figure 4.1. Example of infrared thermography data collection and analysis of images from FLiR i3 handheld camera using ThermaCAM Researcher Professional 2.8 SR-2 software.

[2]Details on the technical characteristics of the camera are provided online at https://doi.org/10.1371/journal.pone.0280098.s001.

analyses in our study. Thermograph resolution was calibrated to ambient temperature before each collection session using a Reed LM-800 4-in-1 pocket thermo-anemometer, hygrometer, thermometer, and illuminometer (Reed Instruments).

Statistical Analyses

Statistical analyses were conducted using RStudio Version 1.3.1093 (RStudio Team, 2020; R Core Team, 2021). Statistical significance was declared at $P < 0.05$. Handling of the collected data for analysis of the different objectives is detailed in Figure 4.2.

First, descriptive analyses were done to identify the number of feet with M2 lesions with IRTmax available after software processing of the infrared thermography images. At the first visit, 21 hind feet met these requirements in the unwashed and washed condition. Another 15 unwashed and 19 washed hind feet were available from the other visits. Because of the low prevalence of M2 lesions in the dataset, it was decided to complement the data from the first visit with M2 scored feet only from the following visits for further statistical analyses.

Prior to statistical analyses, lower leg cleanliness scores and locomotions scores were dichotomized. Dichotomization of the lower leg cleanliness scores was based on presence of dried manure or not, with scores 1 and 2 categorized as 'fresh manure' and scores 3 and 4 as 'dried manure' (Relun et al., 2013b). Dichotomization of the locomotion scores was based on presence of limping indicating lameness with scores 1 and 2 as 'not lame' and scores 3, 4, and 5 as 'lame' (Solano et al., 2016b; van Huyssteen et al., 2020). Associations were first assessed using univariable logistic regression analyses between digital dermatitis status and IRTmax, lower leg cleanliness score, locomotion score, and farm, respectively; and second using multivariable logistic regression analysis. The dependent variable was digital dermatitis status (M2 = 1 and M0IM1IM3IM4 = 0; or digital dermatitis present = 1 and absent = 0) and independent variables were IRTmax, lower leg cleanliness score, and locomotion score. Farm was fixed into the model as a means to account for farm effect and clustering of cows within farm. The final reduced model was based on the lowest Akaike information criterion using a

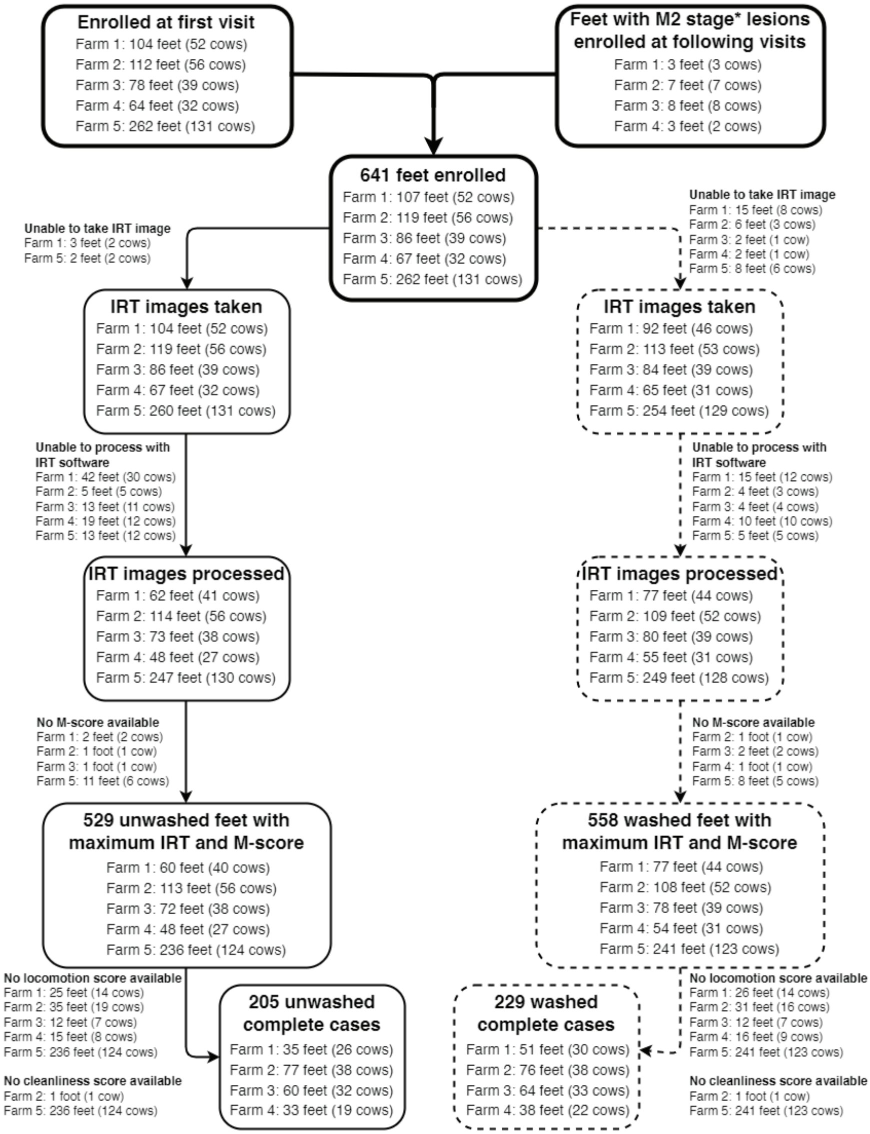

Figure 4.2. Study flow diagram for a study testing the association between broad spectrum infrared thermography and the presence of digital dermatitis lesions using unwashed and washed hind feet from five Canadian dairy herds. The first four herds were visited at three-week intervals for a total of 12 weeks, resulting in five visits with data collection per farm and the fifth farm was visited once. The bold lines represent general study recruitment, the solid lines represent the unwashed hind feet and the dotted lines represent the washed hind feet. The diagram was created with www.app.diagrams.net.

backward elimination approach (Dohoo et al., 2014). Univariable logistic regression analyses used both the full categorical and dichotomized lower leg cleanliness scores and locomotion scores, and results hereof informed variable selection for the multivariable models. To further our understanding of IRTmax within digital dermatitis status, we divided IRTmax into two groups over the median value of IRTmax, regardless of M-score, in the datasets of unwashed and washed feet, respectively, and repeated the multivariable logistic regression analyses as described above. The full results of the regression analyses are reported online at https://doi.org/10.1371/journal.pone.0280098.s002 for M2 lesions and at https://doi.org/10.1371/journal.pone.0280098.s003 for any digital dermatitis lesion.

RESULTS

A total of 641 hind feet from 310 cows of five farms were enrolled in the study (Figure 4.2). After discarding feet missing an IRTmax value, either due to absence of an infrared thermography image or inability to process the infrared thermography image with the software, and discarding feet missing an M-score, a total of 529 unwashed hind feet from 285 cows and a total of 558 washed hind feet from 289 cows with an IRTmax value and an M-score were available for analysis. The unwashed dataset had 54 cows with one observation, 218 cows with two observations, and 13 cows with three observations with IRTmax and M-score data, whereas the washed dataset had 32 cows with one observation, 245 cows with two observations, and 12 cows with three observations with IRTmax and M-score data. From these, 205 unwashed hind feet from 115 cows and 229 washed hind feet from 123 cows also had both lower leg cleanliness score and locomotion score data available.

Lactating herd size ranged from 166 to 279 cows and farm-level digital dermatitis prevalence (at least one hind foot with digital dermatitis) in enrolled cows ranged from 62 to 85% (mean 72%, standard deviation 9) at the first visit. An overview of the M-scores by farm, lower leg cleanliness scores, and locomotion scores for the hind feet with an IRTmax in our study is provided in Table 4.1 and Table 4.2. The unwashed hind feet dataset contained 36 feet with an M2 lesion and 493 feet without an M2 lesion, and 310 feet with digital dermatitis and 219 feet without digital dermatitis. The washed hind feet dataset contained 40 feet with an M2 lesion and 518 feet without an M2 lesion, and 329 feet with digital dermatitis and 229 feet without digital dermatitis. Table 4.3 provides an overview of the descriptive statistics of IRTmax for each group of hind feet and boxplots of the IRTmax are provided in Figure 4.3.

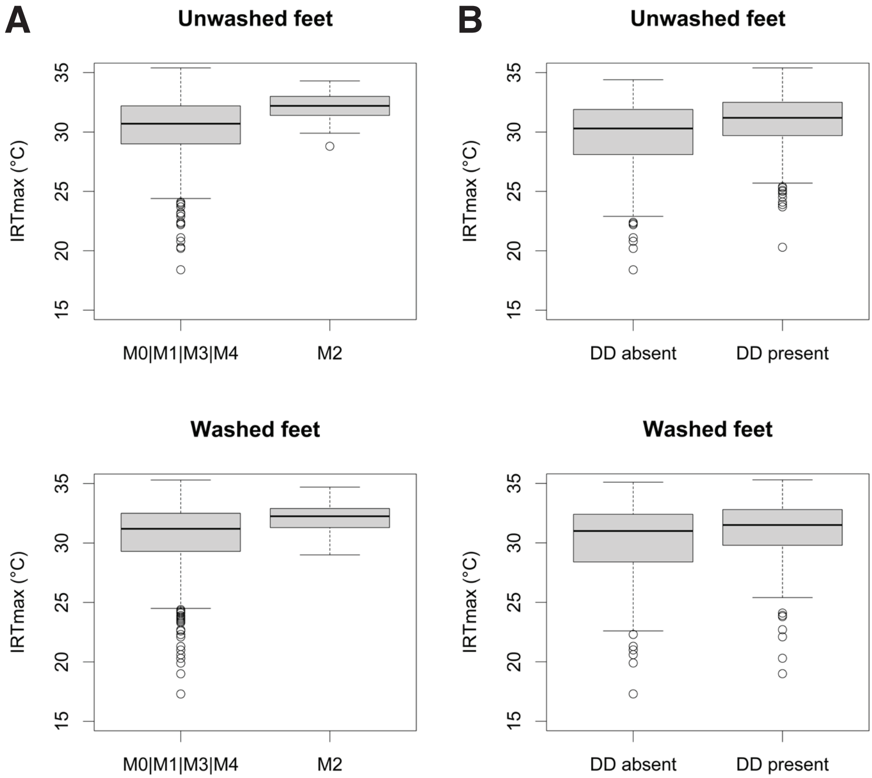

Figure 4.3. Boxplots for maximum infrared temperature (IRTmax) from the pastern region of dairy cattle hind feet before and after washing. (A) For hind feet with M2 or M0IM1IM3IM4 lesions of digital dermatitis (DD). (B) For hind feet with absence or presence of DD. Bold solid line = median, box = interquartile range (IQR), bottom whisker = 25[th] percentile - 1.5 x IQR, top whisker = 75[th] percentile + 1.5 x IQR, circle = datapoint outside the interwhisker range.

Table 4.1. M-scores[1] for digital dermatitis, locomotion score, and cleanliness score for unwashed hind feet with a maximum infrared thermography temperature reading from five Canadian dairy herds

		Unwashed hind feet					
		M0	M1	M2	M3	M4	Total
Herd	1	22	0	2	21	15	60
	2	27	1	14	50	21	113
	3	36	1	7	13	15	72
	4	15	0	1	28	4	48
	5	119	2	12	33	70	236
	Total	219	4	36	145	125	529
Locomotion score[2]	1	45	1	10	57	20	133
	2	10	0	6	20	7	43
	3	7	0	0	8	6	21
	4	4	0	2	2	0	8
	5	0	0	0	0	1	1
	Total	66	1	18	87	34	206
Cleanliness score[3]	1	10	0	2	8	6	26
	2	61	2	7	66	29	165
	3	26	0	14	34	20	94
	4	3	0	0	4	0	7
	Total	100	2	23	112	55	292

[1]M-stages (Döpfer et al., 1997) were determined in-parlor, after washing the feet with water. The M4.1-stage by Berry et al. (2012) is included in the M1-stage.
[2]Locomotion scores (Flower and Weary, 2006) were determined from video recordings of cows exiting the milking parlor with score ≥3 considered lame; only available for feet from farm 1 to 4.
[3]Lower leg cleanliness scores (Cook, 2006; Solano et al., 2015) were determined in-parlor with presence of dried manure in score ≥3; only available for feet from farm 1 to 4.

Table 4.2. M-scores[1] for digital dermatitis, locomotion score, and cleanliness score for washed hind feet with a maximum infrared thermography temperature reading from five Canadian dairy herds

		Washed hind feet					
		M0	M1	M2	M3	M4	Total
Herd	1	32	0	3	24	18	77
	2	23	1	13	51	20	108
	3	36	1	9	15	17	78
	4	14	0	3	32	5	54
	5	124	2	12	34	69	241
	Total	229	4	40	156	129	558
Locomotion score[2]	1	49	1	12	60	23	145
	2	11	0	6	19	8	44
	3	11	0	2	11	8	32
	4	4	0	2	3	0	9
	5	0	0	0	0	0	0
	Total	75	1	22	93	39	230
Cleanliness score[3]	1	6	0	2	10	6	24
	2	65	2	6	73	32	178
	3	32	0	19	36	22	109
	4	2	0	0	3	0	5
	Total	105	2	27	122	60	316

[1]M-stages (Döpfer et al., 1997) were determined in-parlor, after washing the feet with water. The M4.1-stage by Berry et al. (2012) is included in the M1-stage.
[2]Locomotion scores (Flower and Weary, 2006) were determined from video recordings of cows exiting the milking parlor with score ≥3 considered lame; only available for feet from farm 1 to 4.
[3]Lower leg cleanliness scores (Cook, 2006; Solano et al., 2015) were determined in-parlor with presence of dried manure in score ≥3; only available for feet from farm 1 to 4.

Table 4.3. Descriptive statistics for maximum infrared temperature (˚C) of the plantar pastern from standing dairy cattle feet before and after washing, categorized by digital dermatitis status

Digital dermatitis status	N	Mean	SD	Minimum	Q1	Median	Q3	Maximum
Unwashed hind feet								
M2[1]	36	32.1	1.2	28.8	31.5	32.2	33.0	34.3
M0IM1IM3IM4[1]	493	30.3	2.8	18.4	29.0	30.7	32.2	35.4
Digital dermatitis present	310	30.9	2.4	20.3	29.7	31.2	32.5	35.4
Digital dermatitis absent	219	29.7	3.1	18.4	28.1	30.3	31.9	34.4
Washed hind feet								
M2[1]	40	32.1	1.3	29.0	31.3	32.3	32.9	34.7
M0IM1IM3IM4[1]	518	30.5	3.0	17.3	29.3	31.2	32.5	35.3
Digital dermatitis present	329	31.1	2.4	19.0	29.8	31.5	32.8	35.3
Digital dermatitis absent	229	29.9	3.4	17.3	28.4	31.0	32.4	35.1

[1]M-stages (Döpfer et al., 1997) were determined in-parlor, after washing the feet with water; the M4.1-stage by Berry et al. (2012) is included in the M1-stage.

Association of Maximum Infrared Temperature with the Presence of M2 Lesions

In the final multivariable logistic regression analysis models of our study, higher IRTmax values were associated with an increased odds for M2 lesions on both unwashed (adjusted OR 1.6; 95% CI 1.2 to 2.2; Table 4.4) and washed hind feet (adjusted OR 1.4; 95% CI 1.1 to 1.7; Table 4.5), as was presence of dried manure on the lower hind legs (lower leg cleanliness score = 3 and 4; Table 4.4 and 4.5). These associations remained similar after dichotomization of IRTmax with an adjusted odds ratio of 13.9 (95% CI 3.4 to 95.7; Table 4.4) and 4.8 (95% CI 1.7 to 15.8; Table 4.5) for unwashed and washed hind feet, respectively.

Association of Maximum Infrared Temperature with the Presence of Digital Dermatitis Lesions

Multivariable logistic regression analyses identified that higher IRTmax values were associated with an increased odds for digital dermatitis presence on both unwashed (adjusted OR 1.1; 95% CI 1.1 to 1.2; Table 4.6) and washed hind feet (adjusted OR 1.1; 95% CI 1.1 to 1.2; Table 4.7). This association disappeared after dichotomization of IRTmax.

Table 4.4. Final reduced multivariable logistic regression models to test the association between maximum infrared temperature (IRTmax) from the plantar pastern and presence of M2 lesions (Döpfer et al., 1997) of digital dermatitis on unwashed hind feet from standing dairy cattle, with lower leg cleanliness score (CS; Cook, 2006; Solano et al., 2015) as explanatory variable and farm as fixed effect

		Unwashed hind feet	
Model	Variable	Adjusted OR	95% CI
Continuous IRTmax + CS + farm			
	IRTmax	1.6	1.2–2.2
	CS fresh manure	1	Referent
	CS dried manure	4.1	1.6–10.7
	Farm 1	1	Referent
	Farm 2	2.1	0.5–14.2
	Farm 3	5.5	1.2–40.5
	Farm 4	0.4	0.1–4.9
Dichotomized IRTmax[1] + CS + farm			
	IRTmax <31.0˚C	1	Referent
	IRTmax ≥31.0˚C	13.9	3.4–95.7
	CS fresh manure	1	Referent
	CS dried manure	4.0	1.6–10.8
	Farm 1	1	Referent
	Farm 2	2.2	0.5–15.2
	Farm 3	6.4	1.3–48.7
	Farm 4	0.5	0.1–5.6

[1]IRTmax was divided into two groups over the median value of IRTmax, regardless of M-score (Döpfer et al., 1997), in the dataset of unwashed feet.

Table 4.5. Final reduced multivariable logistic regression models to test the association between maximum infrared temperature (IRTmax) from the plantar pastern and presence of M2 lesions (Döpfer et al., 1997) of digital dermatitis on washed hind feet from standing dairy cattle, with lower leg cleanliness score (CS; Cook, 2006; Solano et al., 2015) as explanatory variable and farm as fixed effect

		Washed hind feet	
Model	Variable	Adjusted OR	95% CI
Continuous IRTmax + CS + farm			
	IRTmax	1.4	1.1–1.7
	CS fresh manure	1	Referent
	CS dried manure	5.3	2.2–14.1
	Farm 1	1	Referent
	Farm 2	3.9	1.1–17.9
	Farm 3	10.7	2.7–56.0
	Farm 4	1.9	0.3–11.4
Dichotomized IRTmax[1] + CS + farm			
	IRTmax <31.3˚C	1	Referent
	IRTmax ≥31.3˚C	4.8	1.7–15.8
	CS fresh manure	1	Referent
	CS dried manure	5.5	2.3–14.5
	Farm 1	1	Referent
	Farm 2	4.0	1.2–18.5
	Farm 3	9.4	2.4–48.4
	Farm 4	2.0	0.3–11.4

[1]IRTmax was divided into two groups over the median value of IRTmax, regardless of M-score (Döpfer et al., 1997), in the dataset of washed feet.

Table 4.6. Final reduced multivariable logistic regression models to test the association between maximum infrared temperature (IRTmax) from the plantar pastern and presence of any lesions of digital dermatitis on unwashed hind feet from standing dairy cattle, with farm as fixed effect

		Unwashed hind feet	
Model	Variable	Adjusted OR	95% CI
Continuous IRTmax + farm			
	IRTmax	1.1	1.1–1.2
	Farm 1	1	Referent
	Farm 2	1.4	0.7–2.8
	Farm 3	0.7	0.3–1.4
	Farm 4	1.2	0.6–2.8
	Farm 5	0.6	0.3–0.9
Dichotomized IRTmax[1] + farm			
	IRTmax <31.0˚C	1	Referent
	IRTmax ≥31.0˚C	1.4	0.9–2.1
	Farm 1	1	Referent
	Farm 2	1.6	0.8–3.2
	Farm 3	0.6	0.3–1.2
	Farm 4	1.3	0.6–2.9
	Farm 5	0.6	0.3–0.9

[1]IRTmax was divided into two groups over the median value of IRTmax, regardless of M-score (Döpfer et al., 1997), in the dataset of unwashed feet.

Table 4.7. Final reduced multivariable logistic regression models to test the association between maximum infrared temperature (IRTmax) from the plantar pastern and presence of any lesions of digital dermatitis on washed hind feet from standing dairy cattle, with farm as fixed effect

		Washed hind feet	
Model	Variable	Adjusted OR	95% CI
Continuous IRTmax + farm			
	IRTmax	1.1	1.1–1.2
	Farm 1	1	Referent
	Farm 2	2.7	1.4–5.2
	Farm 3	1.3	0.7–2.7
	Farm 4	2.4	1.1–5.4
	Farm 5	0.8	0.5–1.4
Dichotomized IRTmax[1] + farm			
	IRTmax <31.3˚C	1	Referent
	IRTmax ≥31.3˚C	1.2	0.8–1.7
	Farm 1	1	Referent
	Farm 2	2.6	1.4–5.1
	Farm 3	0.9	0.5–1.7
	Farm 4	2.1	1.0–4.7
	Farm 5	0.7	0.4–1.2

[1]IRTmax was divided into two groups over the median value of IRTmax, regardless of M-score (Döpfer et al., 1997), in the dataset of washed feet.

DISCUSSION

This multi-farm study provides insights into the practical application of infrared thermography for detection of digital dermatitis, M2 lesions in particular, on hind feet from standing cows with a handheld infrared thermography camera. Higher IRTmax values were associated with feet with M2 lesions or digital dermatitis lesions, in comparison with feet without an M2 lesion or without digital dermatitis, respectively, regardless of the hygienic condition of the feet. Dichotomization of IRTmax substantially enlarged the 95% confidence interval for the association with feet with M2 lesions indicating that the association becomes less reliable. When looking at feet with any digital dermatitis lesion, there was no association with the dichotomized IRTmax. Previous work reported poor test characteristics to diagnose the presence of digital dermatitis lesions using IRTmax with sensitivities ranging from 0.75 to 0.89 and specificities ranging from 0.65 to 0.70 (Alsaaod et al., 2014; Anagnostopoulos et al., 2021a). Altogether, these findings suggest that it is unlikely that a cut-off value for IRTmax with high sensitivity and specificity for the detection of feet with M2 lesions can be determined using cross-sectional data.

In analogy with machine learning techniques used for automated mastitis or estrus detection (Reith and Hoy, 2018; Steele et al., 2020), similar techniques can be developed to use IRTmax for the detection of M2 lesions in which the IRTmax from a foot is compared with rolling averages of the same foot, contralateral foot, feet average within cow, herd average, or a combination of these. To date, the authors are unaware of publications that report investigations of this option.

A limitation of this study was the low prevalence of feet with M2 lesions and of lame feet. Although this is a realistic reflection of the average Canadian dairy herd (Jacobs et al., 2018; van Huyssteen et al., 2020), it resulted in a statistically unbalanced dataset. It is possible that this restricted the capacity of our study to detect an association with IRTmax. Also, our dataset contained a large number of animals with only one observation, making the inclusion of cow as a random effect, to account for repeated measures and cows having more than one observation, in our models impossible.

The M-score of the feet in this study was determined by visual inspection of the feet in the milking parlor. Although visual detection of M-scores in the milking parlor versus in the trimming chute was validated (Solano et al., 2017a), we hereby compared IRTmax with an imperfect diagnostic test. Potentially, IRTmax could have correctly diagnosed some feet with M2 lesions that were misclassified as feet without M2 lesions by the in-parlor M-scoring due to the limited sensitivity (0.62) of in-parlor M-scoring for M2 lesions (Solano et al., 2017a). Diagnosis of digital dermatitis in the trimming chute would have reduced possible misclassification of M-scores. Additionally, information on the presence of other foot lesions, such as claw horn lesions, could have been collected as feet with other foot lesions typically tend to have higher IRTmax values compared to feet with no lesions (Alsaaod and Büscher, 2012; Main et al., 2012; Stokes et al., 2012b; Wood et al., 2015). However, inspection of feet in a trimming chute would have neglected the need for an easy, practical method. Higher IRTmax values from cattle feet have also been associated with higher ambient temperatures (Alsaaod and Büscher, 2012; Wood et al., 2015), stage of lactation ≤200 days in milk (Alsaaod and Büscher, 2012), and more recently with higher locomotion scores in a herd without digital dermatitis (Werema et al., 2021). Some of these factors will have been captured by fixing farm into the models, but it is likely that they exert an unmeasured effect on the results of our study.

Further research should aim to include all above-mentioned factors with a preference for longitudinal studies to better evaluate infrared thermography as an early detection method for M2 lesions resulting in lameness. However, these multiple factors which influence the ability to detect M2 lesions, and foot lesions in general, all need to be automatically measured and considered before infrared thermography can be easily used as a detection tool on farm. Until this further research is done, the main potential use of infrared thermography in automated detection of foot health status is likely limited to identify ‘feet at risk’ that need further attention. At-risk feet could either be visually appraised in the trimming chute, or by computer vision and machine learning technology. The YOLOv2 computer vision model of Cernek et al. (2020) correctly classified about 60% of the lesions as an M2 lesion on washed hind feet in an external validation trial on a commercial US dairy herd. Combining infrared thermography with other automated lameness detection devices presumably aids in the identification of feet at risk of compromised foot health.

CONCLUSIONS

The presence of M2 lesions on hind feet was associated with higher IRTmax values of the plantar pastern, both on unwashed and washed feet from standing dairy cattle. Dichotomization of IRTmax substantially decreased the reliability of this association, making it unlikely that IRTmax alone can be used for automated detection of feet with an M2 lesion. It is probable that IRTmax does have a role in identifying feet at risk for compromised foot health that need further checking and thereby is a tool that can aid in the automation of monitoring the foot health status on dairy herds.

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COMPETING INTERESTS

The authors have declared that no competing interests exist.

Chapter 5

M-score and Wound Healing of Digital Dermatitis

Vanhoudt, A., J. Hesseling, M. Nielen, J. Wilmink, R. Jorritsma, and T. van Werven. (2022) M-score and wound healing assessment of 2 non-antibiotic topical gel treatments of active digital dermatitis lesions in dairy cattle. J. Dairy Sci. 105:695–709. doi:10.3168/jds.2021-20613.

ABSTRACT

This open-label, randomized clinical trial with positive control compared the treatment of active digital dermatitis lesions (stages M1, M2, and M4.1) on dairy cattle hind feet with an enzyme alginogel or a copper and zinc chelate gel (coppergel). Upon recruitment (day 0), active digital dermatitis lesions were cleaned, photographed, treated, and bandaged. This procedure was repeated on day 3 and day 7, with treatment and bandaging discontinued for those lesions that had transitioned to the M0-, M3-, or M4-stage on day 7. Day 10 was considered the end of the treatment trial, and all recruited feet were cleaned and photographed. Treatment effect of the two products was assessed not only using the M-score but also using general wound healing progress criteria. Improvement of M-score was defined as transition to M0-, M3-, or M4-stages, or to lesions with a smaller ulcerative area (e.g., M2-stage to M1-stage). Lesions with improved wound healing had at least one of the following criteria when compared with the previous observation: decreased defect size, healthier granulation tissue color (pink-red instead of purple-grayish), more regular aspect of granulation tissue surface, wound contraction, or epithelialization starting from the surrounding skin. Both primary outcomes were assessed using a multivariable logistic regression analysis. Lesions treated with the enzyme alginogel had a decreased adjusted odds ratio for M-score improvement (aOR: 0.04; 95% CI: 0.01 to 0.11). Lesions treated with the coppergel mostly transitioned to chronic lesions, whereas lesions treated with the enzyme alginogel mostly remained active lesions. The wound healing progress of almost 70% of the lesions treated with coppergel could not be scored, for the greater part due to the presence of crust materials. With these unscorable lesions classified as “improved,” there was no treatment effect on wound healing progress (aOR: 0.99; 95% CI: 0.34 to 3.05), whereas with unscorable lesions classified as “not improved,” the enzyme alginogel outperformed the coppergel with regard to wound healing progress (aOR: 2.48; 95% CI: 1.07 to 5.79). None of the products used in our study achieved high cure rates (transition to the M0-stage) for active digital dermatitis lesions. Low cure rates of topical treatment of digital dermatitis, together with the important role of chronic lesions in the epidemiology of digital dermatitis, indicate that future research

should investigate how to achieve successful wound management of digital dermatitis lesions, thereby mitigating pain associated with the lesions and reducing both transmission and prevalence of digital dermatitis within herds.
Key words: digital dermatitis, randomized clinical trial, non-antibiotic, enzyme alginogel, wound management

INTRODUCTION

Digital dermatitis is considered a contagious disease and an important cause of lameness in dairy cattle worldwide. It is characterized by hyperkeratotic or ulcerative lesions, typically located on the plantar or palmar aspect of the foot, immediately proximal to the interdigital cleft. Lesions are mostly present on the hind feet and are associated with lameness, reduced milk production, diminished reproductive performance, and decreased animal welfare (Bruijnis et al., 2012a; Higginson Cutler et al., 2013; Dolecheck and Bewley, 2018).

Ulcerative lesions are commonly grouped as active lesions and consist of the M1-, M2-, and M4.1-stage lesions, whereas M3- and M4-stage lesions are considered chronic lesions (Zinicola et al., 2015b; Biemans et al., 2018). In general, alongside herd-level digital dermatitis control through foot bathing, cows with active digital dermatitis lesions receive a topical treatment with or without bandage (Plummer and Krull, 2017). Topical treatments contain either antibiotics (e.g., broad-spectrum tetracyclines) or a non-antibiotic active compound (e.g., copper and zinc chelates). Products based on copper and zinc chelates are widely used in the Netherlands and are reported as an effective treatment option for digital dermatitis compared with topical tetracyclines, with cure rates of 85 to 90% versus 45 to 55%, respectively (Holzhauer et al., 2011; Dotinga et al., 2017). These cure rates do not necessarily imply return to normal, unaffected skin, but mostly resemble progress of the lesion to a chronic, non-ulcerative, hyperkeratotic M-stage. With this approach, the disease is kept in a manageable state (Döpfer and Bonino Morlán, 2008).

The lesions of digital dermatitis can also be considered chronic, non-healing wounds with a bacterial infection. Second-intention wound healing is a complex interaction between several cell types, the extracellular matrix, and mediators that coordinate the process. This process can arbitrarily be differentiated into four phases: hemostasis, acute inflammation, proliferation, and remodeling (Theoret, 2017). Wound healing evaluation often involves repeated assessments of the size of the lesion (occurrence of wound contraction and epithelialization) and presence of clinical signs that can promote or indicate local infection, such as tissue necrosis, unhealthy granulation tissue (friable, purple or grayish color, irregular aspect), exudation, pocketing, undermining of skin, or sometimes only delayed healing (Lazarus et al., 1994; Theoret, 2017). Management of chronic, open wounds is based on the TIME principle (tissue debridement, infection control, moisture balance, and edges of the wound) and aims at return to normal unaffected skin or a functional epithelial scar (Schultz et al., 2003; Leaper et al., 2012; Bowers and Franco, 2020). Since its first introduction, novel products and strategies have emerged to aid in achieving the TIME principle, with enzymatic alginates being one of them. Recently, an enzyme alginogel has appeared effective in the treatment of udder cleft dermatitis, an ulcerative dermatitis, in dairy cows (van Werven et al., 2018). Alginates are known for their capacity to absorb debris and exudate (passive debridement) and for keeping wounds moist through their gelling capacity (moisture balance; Strohal et al., 2013; Jacobsen, 2017; Jones and Oates, 2018). The alginates in the alginogel absorb bacteria into the gel matrix. In this matrix, the antimicrobial enzyme system of glucose oxidase, lactoperoxidase, and guaiacol (**GLG-enzyme system**) effects a controlled release of reactive oxygen species, which selectively disrupt bacterial cell walls (infection control; De Smet et al., 2009).

We hypothesized that an enzyme alginogel is an effective topical treatment for wound healing of active digital dermatitis lesions. To test this hypothesis, we compared the enzyme alginogel with the standard non-antibiotic topical treatment used in the Netherlands, a copper and zinc chelates gel. Effectiveness of treatment was evaluated using both the M-score for digital dermatitis (Döpfer et al., 1997; Berry et al., 2012) and wound healing criteria (Theoret, 2017).

MATERIALS AND METHODS

Ethical Statement

This study was performed in conformation with European law concerning the protection of animals kept for farming purposes (Council Directive 98/58/EC) and was not considered an animal experiment under Dutch legislation. Farmers participated in the research based on an informed consent statement.

Study Design

This open-label, randomized clinical trial with positive control was set up as an intention-to-treat, non-inferiority trial to compare the treatment of active digital dermatitis lesions with an enzyme alginogel [treatment group (alginogel), BoTop, Flen Health; none of the components require a maximum residue level, and therefore there is no authorization number nor withdrawal period] or with a copper and zinc chelates gel [control group (coppergel), Intra Hoof-fit Gel, Intracare; authorization number RegNL 109438, 0-d withdrawal period for both milk and meat]. For welfare reasons, an untreated negative control group was not included in the study design. Randomization was blocked by farm with pseudorandomization at cow level by flipping a coin for the first cow with an active digital dermatitis lesion on each farm. Sample size was calculated a priori using the Farrington-Manning score test for proportion difference in SAS (version 9.4M5, SAS Institute Inc.), with a difference greater than 10% indicating inferiority. The expected M-score improvement rate of the coppergel was set at 92% (Holzhauer et al., 2011). Considering a 95% confidence interval and a power of 80% resulted in a calculated sample size of at least 104 active digital dermatitis lesions in each group.

Scorer Training

Four students in veterinary medicine were trained in applying the M-score (Döpfer et al., 1997; Berry et al., 2012) by studying the literature, classroom training (39 digital color photographs of cattle feet with varying M-stages, 61% agreement between the four scorers), and one in-parlor M-scoring of washed hind feet of approximately 50 dairy cows together with the first author (Relun et al., 2011; Solano et al., 2017a).

Herd Selection

Veterinarians working in the Utrecht area were contacted and asked to suggest dairy farms that would meet the selection criteria for the study: (1) herds estimated to have a high (>20%) prevalence of cows with active digital dermatitis lesions, (2) presence of a safe and functional trimming chute on the farm, (3) lactating herd size of at least 50 cows, and (4) willingness to participate in the study. This resulted in a convenience sample of seven farms. Farms were recruited between January 20 and February 20, 2019.

Treatment Protocol

At each M-score assessment of the feet, a spreading plier was available to allow inspection of the interdigital cleft. All treatments were applied by trained veterinary students. Upon recruitment (day 0), on all farms but one, the hind feet of all lactating cows were given a foot trim according to the Dutch five-step method (Toussaint Raven, 1989) by the herd's regular hoof trimmer and all feet of these cows were given an M-score by a trained veterinary student. On one farm (farm 1), the farmer selected 43 cows (out of 118 lactating cows) for foot trimming, because they were lame, likely to have an active digital dermatitis lesion, or both. Hind feet with an active digital dermatitis lesion (i.e., lesions of stage M1, M2, or M4.1; Zinicola et al., 2015b; Biemans et al., 2018) were selected for topical treatment. The first case on a farm was allocated to the alginogel or coppergel group by flipping a coin. Thereafter, cows were alternately allocated to the alginogel or coppergel group. All active digital dermatitis lesions within one cow received the same treatment, to exclude a potential systemic effect of the treatment product. Before applying a treatment, lesions were cleaned with cold water, a paper towel, or both, and a photograph was taken (Sony Cybershot DSC-W830, Sony). The treatment product was applied directly to the lesion so that it covered the entire lesion, and then the treated lesion was covered with a non-aqueous, non-linting gauze dressing that was impregnated with a water-repellent ointment (Cuticerin gauze dressing, 10 × 10 cm, Smith and Nephew). The foot was then bandaged with soft padding (Cellona, Lohmann and Rauscher), vetwrap (EickWrap, Eickenmeyer), and tape (Leukoplast, BSN Medical; Figure 5.1). On day 3, the bandage was removed in a trimming chute, and the foot was gently rinsed with cold water and dried with a paper towel. The lesion was then given an M-score, photographed, and, irrespective of the M-score on day 3, treated under bandage with the same product that was used on day 0, as described previously. On day 7 this procedure was repeated for

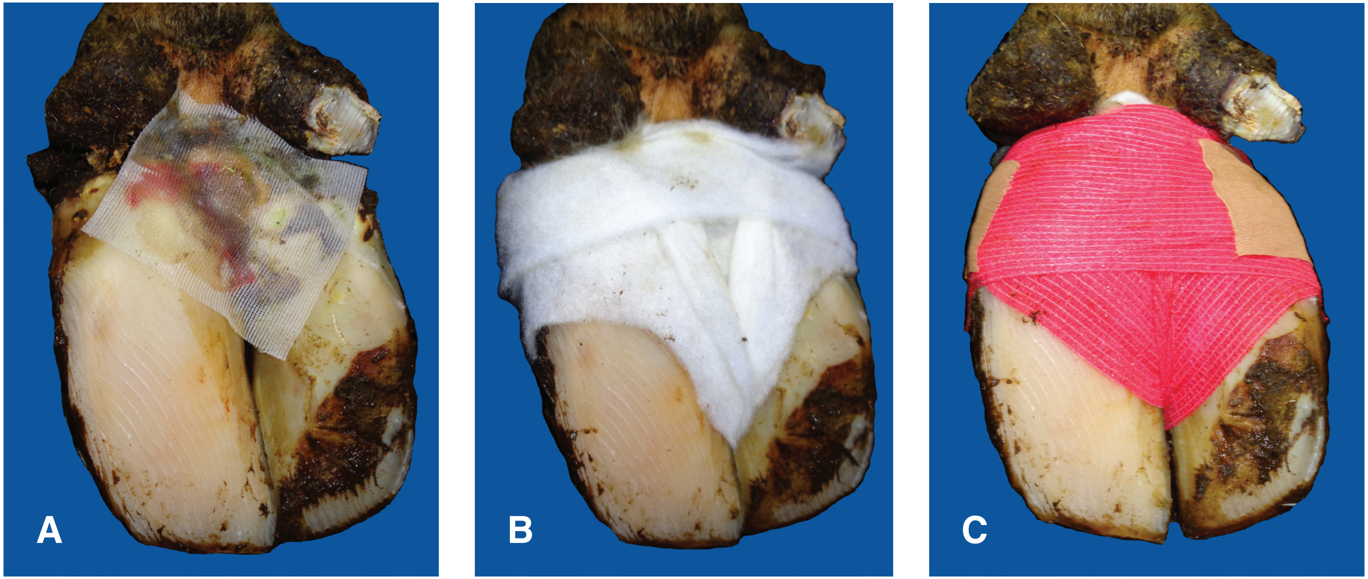

Figure 5.1. The digital dermatitis lesion was fully covered with the treatment product (in this photograph, enzyme alginogel) and covered with an impregnated, non-aqueous, non-linting gauze dressing (A). The foot was then bandaged with a soft padding (B) and with vetwrap and tape (C).

feet with active lesions. Feet without active digital dermatitis lesions on day 7 were only M-scored and photographed, and received no further treatment nor bandage. All feet recruited on day 0 were given a final M-score and photographed on day 10 after rinsing with cold water and drying with a paper towel. Day 10 was considered the endpoint of the treatment period. For welfare reasons, lesions that were still active at day 10 were treated according to the farm treatment protocol, which was mostly a tetracycline spray or the coppergel without bandage. Due to logistical reasons, the day 10 evaluation took place on day 9 on farm 5. The students were aware of the treatment allocation in such a way that they applied and recorded the initial treatment on day 0 and could see the different color of the treatment products (green for coppergel and transparent for alginogel) when replacing the bandage. The students would always first M-score the lesion and then check the treatment allocation of the lesion for further treatment according to the protocol. The treatment allocation of the lesions was masked for the farmers. Farmers were not allowed to run the cows through a footbath during the 10-day trial period.

Treatment Outcomes

M-score. Improvement of M-score, including cure, between day 0 and day 10 (**MS0–10**; Table 5.1) was the primary outcome and was investigated using an M-score transition matrix. Cure was defined as a transition to the M0-stage.

Table 5.1. Definitions of improvement and cure following non-antibiotic topical treatment with bandage of active digital dermatitis lesions using M-scores (Döpfer et al., 1997; Berry et al., 2012) at the start (day 0) and end (day 10) of the treatment trial

	M-score on day 10	
M-score on day 0	Improvement	Cure
M1	M0, M3, and M4	M0
M2	M0, M1, M3, M4, and M4.1	M0
M4.1	M0, M1, M3, and M4	M0

Wound Healing Progress. Treatment allocation of the lesions was masked during the assessment of wound healing progress. An expert in veterinary wound healing (JW) examined all photographs made during the treatment period for skin necrosis, granulation tissue, granulation tissue level in comparison with the surrounding skin, granulation tissue necrosis, wound contraction, and epithelialization. Sequential pairs of photographs of the lesions [i.e., day 0–day 3 (**WH0–3**), day 3–day 7 (**WH3–7**), day 7–day 10 (**WH7–10**), and day 0–day 10 (**WH0–10**, primary outcome)] were given an evaluation of wound healing progress: improved, equal, worsened, or unable to score (Figure 5.2). Lesions with improved wound healing had at least one of the following criteria when compared with the previous observation: decreased defect size, healthier granulation tissue color (pink-red instead of purple-grayish), more regular aspect of granulation tissue surface, wound contraction, or epithelialization starting from the surrounding skin. Wound healing progress that was unable to be scored was specified as presence of crust materials, presence of fecal contamination, poor image quality, or other. The end of the treatment period (day 10) was the endpoint of the wound healing assessment.

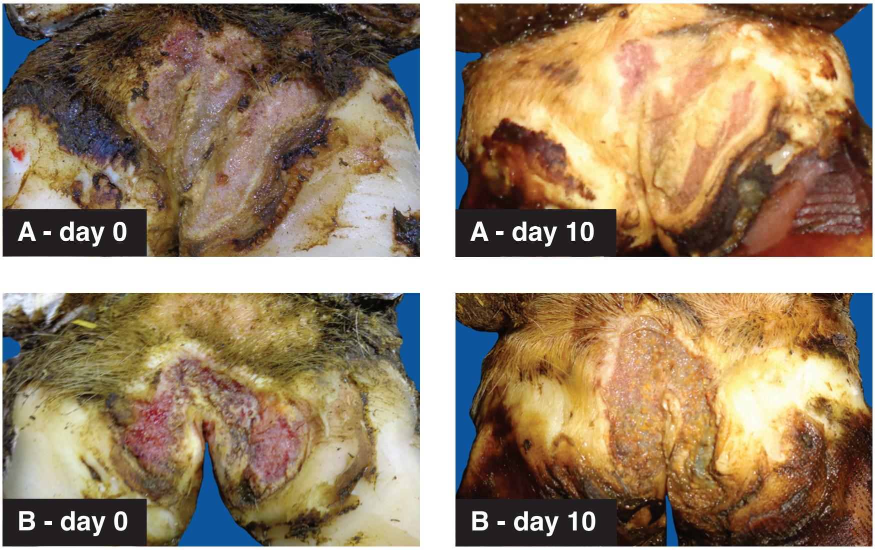

Figure 5.2. Digital photographs of a digital dermatitis lesion treated with enzyme alginogel, with (A) "improved" and (B) "not improved" wound healing progress during the 10-day treatment trial.

Statistical Analysis

Data were analyzed using the statistical software package R (R Core Team, 2021). The experimental unit was a lesion at stage M1, M2, or M4.1 on a hind foot at recruitment (day 0).

M-score. The primary outcome for the M-score was analyzed in a logistic regression analysis of MS0–10 (improved or not improved, using the same definitions as for the M-score treatment outcome; Table 5.1). To enable assessment of the effect of different time periods under bandage (seven versus 10 days), a variable “bandage” was created. First, univariable logistic regression models were applied to assess the effect of treatment, M-score on day 0, bandage, and farm, respectively, on MS0–10. This was followed by a multivariable model with treatment, M-score on day 0, and bandage as independent variables, and farm as fixed effect. The final reduced model was based on the lowest Akaike information criterion using a backward elimination approach (Dohoo et al., 2014).

Wound Healing Progress. The primary outcome for wound healing progress was modeled in a logistic regression analysis of WH0–10 [improved or not improved (i.e., equal, worsened, and unable to score)]. First, univariable logistic regression models were applied to assess the effects of treatment, M-score on day 0, bandage, WH0–3, WH3–7, WH7–10, and farm, respectively, on WH0–10. This was followed by a multivariable model with treatment, M-score on day 0, bandage, WH0–3, WH3–7, and WH7–10 as independent variables, and farm as fixed effect, using the same backward elimination procedure as for the M-score.

RESULTS

Lactating Herd Digital Dermatitis Prevalence on Day 0 and Study Flow

The lactating herd prevalence of active digital dermatitis lesions at feet level on day 0 ranged between 10 and 45% (median: 17%; first quartile: 16%; third quartile: 26%; Figure 5.3). An overview of the study flow of hind feet recruited for the primary outcomes of this study is given in Figure 5.4. In total, 212 and 207 hind feet with active digital dermatitis lesions were analyzed for MS0–10 and WH0–10, respectively.

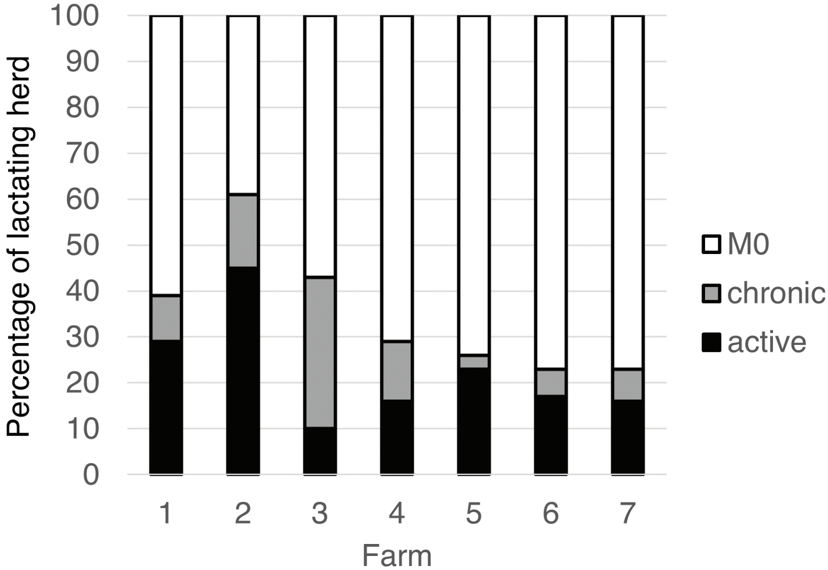

Figure 5.3. Feet-level prevalence of digital dermatitis in the lactating herd at recruitment for the study. Lesions of stages M1, M2, and M4.1 are grouped as active, and lesions of stages M3 and M4 are grouped as chronic (Döpfer et al., 1997; Berry et al., 2012; Zinicola et al., 2015b). For herd 1, prevalence was determined from 43 out of 118 lactating cows, which were selected by the farmer for participation in the study.

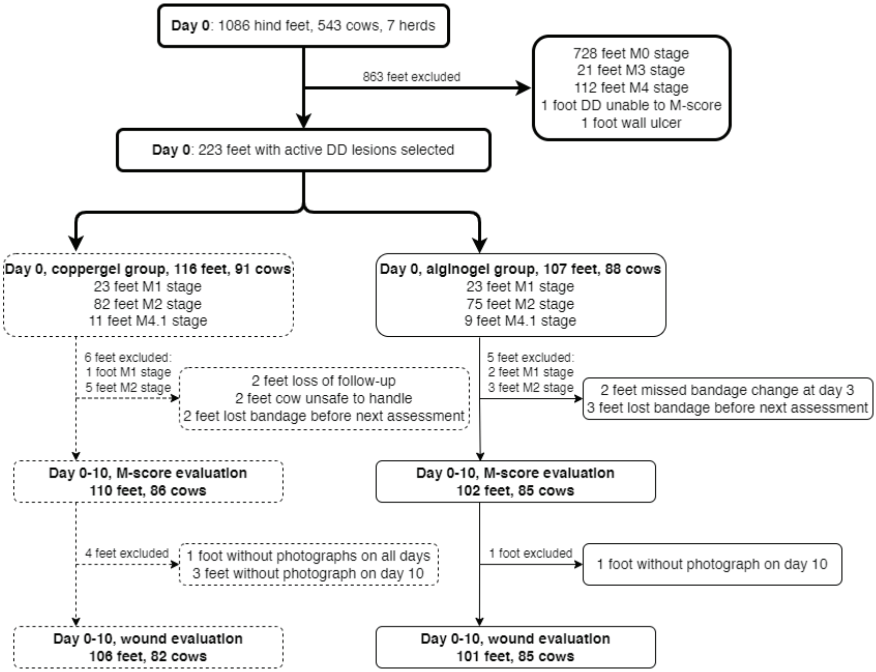

Figure 5.4. REFLECT study flowchart for an open-label, randomized clinical intention-to-treat, non-inferiority trial with positive control assessing the M-score improvement and wound healing progress of active digital dermatitis (DD) lesions (M1, M2, or M4.1 stage; Döpfer et al., 1997; Berry et al., 2012) on hind feet from lactating dairy cows on seven dairy farms, treated with an enzyme alginogel or copper and zinc chelate gel (coppergel) with bandage. Bold solid lines represent general study recruitment; dotted lines represent the coppergel group; and light solid lines represent the alginogel group.

Treatment Outcomes

M-score at Day 10. The overall MS0–10 improvement (M-stage change from active to chronic or healed) was 27% for the alginogel group and 94% for the coppergel group, indicating inferiority of the alginogel at changing lesions from active to chronic or healed M-stages (Table 5.2). Of all treated lesions, 3% were cured (M-stage change from active to healed) by day 10, with 2% cured in the alginogel group and 4% cured in the coppergel group. In the alginogel group, M1-stage lesions mainly remained at M1-stage (33%) or became M2, M3, or M4.1 lesions by day 10, whereas the majority of M2-stage lesions remained M2 lesions (77%). In the coppergel group, however, active digital dermatitis lesions were most likely to become M3-stage lesion (75%) by day 10. The full transition matrix for day 10 M-scores in relation to day 0 M-scores is given in the Appendix (Table A1).

Table 5.2. M-score improvement 10 days after treatment of active digital dermatitis lesions on hind feet from 171 cows on seven dairy farms, with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage[1]

	Alginogel		Coppergel	
M-score[2] on day 0	N	M-score improvement, N (%)	N	M-score improvement, N (%)
M1	21	6 (29)	22	21 (95)
M2	72	17 (24)	77	71 (92)
M4.1	9	5 (56)	11	11 (100)
Total	102	28 (27)	110	103 (94)

[1]M-score improvement was defined as transition to M0-, M3-, or M4-stages or to lesions with a smaller ulcerative area (e.g., M2-stage to M1-stage).
[2]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

Wound Healing Progress. Of the lesions treated with alginogel, 63% improved between day 0 and day 10, indicating inferiority of the coppergel with respect to wound healing progression (Table 5.3). Lesions with improved wound healing at day 10 compared with day 0 matched at least one of the following criteria: decreased defect size, healthier granulation tissue color (pink-red instead of purple-grayish), more regular aspect of granulation tissue surface, wound contraction, or epithelialization starting from the surrounding skin. The WH0–10 for the majority of the lesions treated with the coppergel could not be assessed (68%), mostly due to the presence of crust materials (Table 5.4; Figure 5.5). Of the remaining lesions treated with the coppergel, 21% improved (Table 5.3). The M-scores on day 10 for those feet for which WH0–10 could not be scored are provided in the Appendix (Table A2).

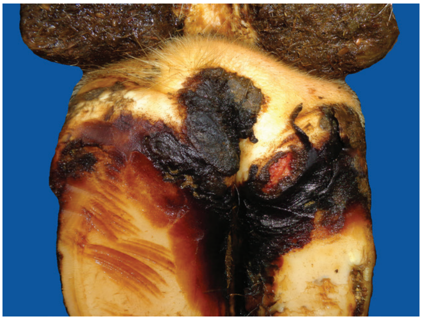

Figure 5.5. Digital color photograph of a digital dermatitis lesion covered with crusts, 10 days after treatment with copper and zinc chelate gel under bandage.

Table 5.3. Overview of wound healing (WH) progress after treatment of active digital dermatitis lesions on hind feet from 167 cows on seven dairy farms, with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage[1]

Evaluation pair, wound healing progress	Alginogel, N (%)	Coppergel, N (%)
N hind feet	101 (100)[2]	106 (100)
WH0–10[3]		
Improved	64 (63)	22 (21)
Equal	27 (27)	10 (9)
Worsened	2 (2)	2 (2)
Unable to score	8 (8)	72 (68)
WH0–3[4]		
Improved	30 (30)	13 (13)
Equal	37 (37)	11 (10)
Worsened	1 (1)	0
Unable to score	32 (32)	82 (78)
WH3–7[5]		
Improved	31 (31)	9 (8)
Equal	33 (33)	8 (8)
Worsened	2 (2)	1 (1)
Unable to score	34 (34)	88 (83)
WH7–10[6]		
Improved	49 (49)	7 (7)
Equal	23 (23)	8 (8)
Worsened	7 (7)	3 (3)
Unable to score	21 (21)	88 (82)

[1]Lesions with improved wound healing had at least one of the following criteria when compared with the previous observation: decreased defect size, healthier granulation tissue color (pink-red instead of purple-grayish), more regular aspect of granulation tissue surface, wound contraction, or epithelialization starting from the surrounding skin. Percentages add up vertically per evaluation pair.
[2]For WH3–7 and WH7–10, the day 7 photograph was missing for one foot.
[3]Primary outcome, wound healing progress between day 0 and day 10.
[4]Wound healing progress between day 0 and day 3.
[5]Wound healing progress between day 3 and day 7.
[6]Wound healing progress between day 7 and day 10.

Table 5.4. Overview of reasons for inability to score wound healing progress between day 0 and day 10 of active digital dermatitis lesions on hind feet from 167 cows on seven dairy farms, after treatment with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage

Item	Alginogel (n = 101) N (%)	Coppergel (n = 106) N (%)	Total (n = 207) N (%)
N hind feet unable to score	8 (100)	72 (100)	80 (100)
Presence of crust materials	0	51 (71)	51 (64)
Presence of fecal contamination	1 (13)	16 (22)[1]	17 (21)
Poor photograph quality	6 (74)	4 (6)	10 (13)
Other	1 (13)	1 (1)	2 (2)

[1]Of these 16 feet, 15 were not bandaged between day 7 and day 10.

Logistic Regression Analyses

M-score. The results of the univariable logistic regression analyses are provided in the Appendix (Table A3). In the final multivariable model, lesions treated with alginogel had a 20-fold decreased odds ratio for M-stage change from active to chronic or healed [improved MS0–10, adjusted odds ratio (**aOR**): 0.04; 95% CI: 0.01 to 0.11; Table 5.5] compared with lesions treated with coppergel.

Wound Healing Progress. To deal with the large proportion of lesions for which WH0–10 could not be scored, these lesions were first classified as "improved" for the logistic regression analyses, followed by classification as "not improved" and repetition of the logistic regression analyses. The results of the univariable logistic regression analyses are provided in the Appendix (Table A3). With unscorable lesions classified as "improved", we found no treatment effect on WH0–10 in the multivariable model (aOR: 0.99; 95% CI: 0.34 to 3.05; Table 5.6). In contrast, with unscorable lesions classified as "not improved", the alginogel WH0–10 outperformed the coppergel (aOR: 2.48; 95% CI: 1.07 to 5.79; Table 5.6).

Table 5.5. Final reduced multivariable logistic regression analysis results for the associations between the dichotomous outcome variable M-score improvement between day 0 and day 10, and different explanatory variables with farm as fixed effect (results not presented)[1]

	M-score improvement[1]	
Variable	aOR[2]	95% CI
Intercept	0.80	
Treatment group		
Coppergel	1	Referent
Alginogel	0.04	0.01–0.11
M-score[3] on day 0		
M1		
M2	3.09	0.79–15.76
M4.1	16.79	2.33–150.61
Period under bandage		
10 days		
7 days	17.92	4.69–98.87

[1]Data were collected from active digital dermatitis lesions on hind feet from 171 cows on seven dairy farms, treated with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage. M-score improvement was defined as transition to M0-, M3-, or M4-stages or to lesions with a smaller ulcerative area (e.g., M2-stage to M1-stage).
[2]Adjusted odds ratio.
[3]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

Table 5.6. Final reduced multivariable logistic regression analysis results for the associations between the dichotomous outcome variable wound healing progress (with unscorable lesions classified as either "not improved" or "improved") between day 0 and day 10, and different explanatory variables with farm as fixed effect (results not presented)[1]

	Wound healing progress[1]			
	Unscorable lesions classified as "not improved"		Unscorable lesions classified as "improved"	
Variable	aOR[2]	95% CI	aOR[2]	95% CI
Intercept	0.10		0.14	
Treatment group				
Coppergel	1	Referent	1	Referent
Alginogel	2.48	1.07–5.79	0.99	0.34–3.05
WH0–3[3]				
Not improved				
Improved			3.67	1.19–11.72
WH3–7[4]				
Not improved				
Improved	8.72	2.72–31.84		
WH7–10[5]				
Not improved				
Improved	27.07	8.71–107.90	41.27	13.60–154.08

[1]Data were collected from active digital dermatitis lesions on hind feet from 167 cows on seven dairy farms, treated with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage. Lesions with improved wound healing had at least one of the following criteria when compared with the previous observation: decreased defect size, healthier granulation tissue color (pink-red instead of purple-grayish), more regular aspect of granulation tissue surface, wound contraction, or epithelialization starting from the surrounding skin.
[2]Adjusted odds ratio.
[3]Wound healing progress between day 0 and day 3.
[4]Wound healing progress between day 3 and day 7.
[5]Wound healing progress between day 7 and day 10.

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DISCUSSION

This study investigated the effect of two non-antibiotic topical treatment products on active digital dermatitis lesions using M-score improvement and wound healing progress as primary outcome measures. It is important to differentiate the M-score classification from wound healing progress classification. The M-score classification system was developed by Döpfer (1994) from a cross-sectional observational study, with histopathological findings of the M-score classes added later (Döpfer et al., 1997). Although the M-score classification system describes the epidemiological progress of digital dermatitis in cows, the classification differs from current understanding of optimal wound healing progress in second-intention healing. Second-intention wound healing is a complex, dynamic process of four strongly interrelated phases (hemostasis, acute inflammatory phase, proliferative phase, and remodeling; Stadelmann et al., 1998; Shearer et al., 2015; Theoret, 2017).

At the end of the 10-day treatment trial, M-score improvement was high for lesions treated with coppergel, with most of the active lesions transitioned into chronic M3- or M4-stage lesions. By contrast, M-score improvement was low for lesions treated with alginogel, with most of the lesions remaining active M1-, M2- , or M4.1-stage lesions. The high M-score improvement of lesions treated with coppergel is in line with findings by others (Holzhauer et al., 2011; Dotinga et al., 2017). Copper has an astringent effect, which dries the lesion and stimulates crust formation, resulting in transition to M3-stage lesions, which is the characteristic reaction to topical treatment products (Döpfer et al., 1997). The alginogel, on the other hand, has a debriding and moisturizing effect (Strohal et al., 2013; Jacobsen, 2017; Jones and Oates, 2018), which apparently results in the majority of the lesions remaining active digital dermatitis lesions during a treatment period of 10 days. It is possible that the treatment period was not long enough for active lesions to transition to chronic or healed M-stages in the alginogel group. For udder clef dermatitis lesions with broken skin barrier, van Werven et al. (2018) reported that median time to first improvement with daily application of alginogel varied between one and four weeks, depending on lesion size, and fewer than 10% of severe udder cleft dermatitis lesions were cured after a 12-week treatment period.

In the final multivariable model, a shorter period under bandage had an increased likelihood for M-score improvement. The protocol for bandage duration was based on M-stage at the intermediate evaluation on day 7, with discontinued treatment (and left without bandage) of M0-, M3-, and M4-stage lesions at day 7. This caused a high correlation between chronic lesions and bandage cessation at day 7. In the coppergel group, 72% were chronic lesions by day 7, whereas in the alginogel group this was only 11% (Appendix, Table A4). Of the M0-, M3-, and M4-stage lesions on day 7 (with discontinued treatment), only 6% had reverted to active digital dermatitis lesions by day 10 (Appendix, Table A4). This low percentage of reversion of chronic or healed lesions to active digital dermatitis lesions is a probable explanation for the positive association between short bandage duration and M-score improvement between day 0 and day 10. Compared with treatment protocols without bandage, other research supports a positive association between bandaging and M-score improvement of digital dermatitis lesions (Higginson Cutler et al., 2013; Klawitter et al., 2019).

One limitation of our study is that, in both treatment groups, about 25% of cows received the same treatment on both hind feet. It is possible that the results of our study are biased by an unmeasured cow effect. When we randomly excluded one foot per cow, the estimates of the final multivariable models were very similar but with larger 95% confidence interval, indicating more uncertainty for the estimates (Appendix, Table A5). Another limitation is the short duration of follow-up in our study. Most other studies incorporated a lesion assessment at day 28 after topical treatment, with lower M-score improvement rates than earlier assessments, due to recrudescence of lesions or development of new lesions (Berry et al., 2010; Holzhauer et al., 2011; Paudyal et al., 2020).

We detected more improved wound healing progress in the alginogel group than in the coppergel group. However, wound healing progress could not be evaluated for a large proportion of lesions in the coppergel group, due to the presence of crust materials. Crusts hamper the assessment of wounds, as removal of the crust might reveal a healthy, healing wound or an infected wound. The presence of crusts in general impedes wound healing, as it delays epithelialization (Kunugiza et al., 2010). The conclusions about the wound healing properties of the two products changed considerably when wounds under crusts were assumed to be improved or not improved.

As neither of these two extremes is likely to be the truth, we suggest that further research on healing of digital dermatitis lesions that avoids the formation of crusts (M3-stage) is needed. Alongside dealing with the aspects of wound healing, new treatment products for digital dermatitis lesions should also be assessed in light of reduction of lesion pain and accompanying lameness.

Digital dermatitis lesions could be considered infected wounds, as bacterial (*Treponema* spp.) contamination and colonization has surpassed the local defense mechanisms of the cow, resulting in interruption of the skin, unhealthy granulation-like tissue, and poor healing progression (Lipsky et al., 2016). In vitro work has identified that exposure of bovine macrophages to *Treponema phagedenis*-like spirochetes impairs their innate immune response and wound repair functions (Zuerner et al., 2007). Topical treatment with dressings with antimicrobial properties can help the immune system to overcome the infection, allowing second-intention wound healing. Copper has good antimicrobial properties but is likely too astringent and results in formation of crusts. The GLG-enzyme system in alginogel has the potential to resolve the infection, but possibly treatment duration in our study was too short to achieve completion of the wound healing process. For both copper and the GLG-enzyme system, efficacy against pathogenic *Treponema* spp. in digital dermatitis still needs to be demonstrated, both in vitro and in vivo.

In general, topical treatment is applied to active lesions of digital dermatitis, as these lesions are most painful (Higginson Cutler et al., 2013). With transition of active lesions to chronic lesions, following topical treatment, the painful aspect of digital dermatitis is usually mitigated, and the disease is kept in a manageable state (Döpfer and Bonino Morlán, 2008). However, chronic M4-stage lesions have been identified as an important source of transmission of digital dermatitis within herds (Biemans et al., 2018). We hypothesize that a topical treatment product and protocol with a swift return to the M0-stage as outcome, instead of the chronic digital dermatitis stages, would not only improve the welfare of the treated cows but likely also help in herd-level digital dermatitis control.

CONCLUSIONS

We investigated the effect of two non-antibiotic topical treatment products on M-score improvement and wound healing progress of active digital dermatitis lesions. Coppergel outperformed alginogel in M-score improvement, resulting in a manageable state of disease, with the majority of lesions remaining in the chronic state. In contrast, the alginogel achieved improved wound healing progress compared with the coppergel. However, none of the products used in our study achieved high cure rates (return to the M0-stage) for active digital dermatitis lesions. Future research is needed to identify what is needed to achieve successful wound management of digital dermatitis lesions and thereby mitigate pain associated with the lesions and reduce both transmission and prevalence of digital dermatitis within herds.

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COMPETING INTERESTS

The authors have not stated any conflicts of interest.

APPENDIX

Table A1. Trimming chute M-score transition matrix of active digital dermatitis lesions on hind feet from 171 cows on seven dairy farms between day 0 and day 10 following treatment with an enzyme alginogel or a copper and zinc chelates gel (coppergel); for each treatment group, percentages add up horizontally per M-score on day 0

	M-score on day 10, N (%)						
Treatment group, M-score[1] on day 0	M0	M1	M2	M3	M4	M4.1	Total
Alginogel							
M1	0	7 (33)	4 (19)	4 (19)	2 (10)	4 (19)	21 (100)
M2	0	11 (15)	55 (77)	2 (3)	3 (4)	1 (1)	72 (100)
M4.1	2 (22)	2 (22)	2 (22)	1 (12)	0	2 (22)	9 (100)
Total	2 (2)	20 (19)	61 (60)	7 (7)	5 (5)	7 (7)	102 (100)
Coppergel							
M1	4 (18)	1 (4)	0	12 (55)	5 (23)	0	22 (100)
M2	1 (1)	6 (8)	6 (8)	63 (82)	1 (1)	0	77 (100)
M4.1	0	1 (9)	0	8 (73)	2 (18)	0	11 (100)
Total	5 (5)	8 (7)	6 (5)	83 (76)	8 (7)	0	110 (100)

[1]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

Table A2. Overview of the M-scores on day 10 per treatment group for feet with photographs classified as "unable to score" for wound healing progress of hind feet with M1, M2, or M4.1 digital dermatitis lesions on day 0 from 167 cows on seven dairy farms, after treatment with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage

	Coppergel group (n = 106)			Alginogel group (n = 101)			Total (n = 207)		
Reason unable to score	Unable to score (N = 72)	M-score[1] day 10	Scored	Unable to score (N = 8)	M-score[1] day 10	Scored	Unable to score (N = 80)	M-score[1] day 10	Scored
Presence of crust materials	51	M0	1	0	M0	0	51	M0	1
		M1	4		M1	0		M1	4
		M2	1		M2	0		M2	1
		M3	45		M3	0		M3	45
		M4	0		M4	0		M4	0
		M4.1	0		M4.1	0		M4.1	0
Presence of fecal contamination	16	M0	0	1	M0	0	17	M0	0
		M1	0		M1	1		M1	1
		M2	0		M2	0		M2	0
		M3	16		M3	0		M3	16
		M4	0		M4	0		M4	0
		M4.1	0		M4.1	0		M4.1	0

[1]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

Table A2 (Continued). Overview of the M-scores on day 10 per treatment group for feet with photographs classified as "unable to score" for wound healing progress of hind feet with M1, M2, or M4.1 digital dermatitis lesions on day 0 from 167 cows on seven dairy farms, after treatment with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage

	Coppergel group (n = 106)			Alginogel group (n = 101)			Total (n = 207)		
Reason unable to score	Unable to score (N = 72)	M-score[1] day 10	Scored	Unable to score (N = 8)	M-score[1] day 10	Scored	Unable to score (N = 80)	M-score[1] day 10	Scored
Poor photograph quality	4	M0	0	6	M0	0	10	M0	0
		M1	2		M1	0		M1	2
		M2	0		M2	3		M2	3
		M3	2		M3	1		M3	3
		M4	0		M4	2		M4	2
		M4.1	0		M4.1	0		M4.1	0
Other	1	M0	0	1	M0	0	2	M0	0
		M1	0		M1	0		M1	0
		M2	0		M2	1		M2	1
		M3	1		M3	0		M3	1
		M4	0		M4	0		M4	0
		M4.1	0		M4.1	0		M4.1	0

[1]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

Table A3. Associations between M-score improvement and wound healing progress between day 0 and day 10 outcome variables and different explanatory variables using univariable logistic regression analysis regardless of farm effect[1]

	M-score improvement[1]	
Variable	Odds ratio	95% CI
Treatment group		
Coppergel	1	Referent
Alginogel	0.03	0.01–0.06
M-score[2] on day 0		
M1	1	Referent
M2	0.85	0.42–1.71
M4.1	2.37	0.72–9.39
Period under bandage		
10 days	1	Referent
7 days	40.29	15.66–140.32

[1]Data were collected from active digital dermatitis lesions on hind feet from 171 cows on seven dairy farms, treated with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage. M-score improvement was defined as transition to M0-, M3-, or M4-stages or to lesions with a smaller ulcerative area (e.g., M2-stage to M1-stage).
[2]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

Table A3 (Continued). Associations between M-score improvement and wound healing progress between day 0 and day 10 outcome variables and different explanatory variables using univariable logistic regression analysis regardless of farm effect[1]

	Wound healing progress[1]			
	Unscorable lesions classified as "not improved"		Unscorable lesions classified as "improved"	
Variable	OR	95% CI	OR	95% CI
Treatment group				
Coppergel	1	Referent	1	Referent
Alginogel	6.60	3.60–12.49	0.32	0.15–0.65
M-score[2] on day 0				
M1	1	Referent	1	Referent
M2	1.17	0.58–2.40	1.85	0.82–4.03
M4.1	1.46	0.48–4.41	2.13	0.57–10.36
Period under bandage				
10 days	1	Referent	1	Referent
7 days	0.25	0.13–0.46	1.59	0.79–3.32
WH0–3[3]				
Not improved	1	Referent	1	Referent
Improved	4.45	2.19–9.47	4.96	2.39–10.41
WH3–7[4]				
Not improved	1	Referent	1	Referent
Improved	12.42	5.24–34.53	5.92	2.79–12.73
WH7–10[5]				
Not improved	1	Referent	1	Referent
Improved	44.35	16.69–154.49	33.83	14.14–88.00

[1]Data were collected from active digital dermatitis lesions on hind feet from 167 cows on seven dairy farms, treated with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage. Lesions with improved wound healing had at least one of the following criteria when compared with the previous observation: decreased defect size, healthier granulation tissue color (pink-red instead of purple-grayish), more regular aspect of granulation tissue surface, wound contraction, or epithelialization starting from the surrounding skin.
[2]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).
[3]Wound healing progress between day 0 and day 3.
[4]Wound healing progress between day 3 and day 7.
[5]Wound healing progress between day 7 and day 10.

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Table A4. Trimming chute M-score serial transition matrix of active digital dermatitis lesions on hind feet from 171 cows on seven dairy farms between day 0, day 3, day 7, and day 10 following treatment with an enzyme alginogel (alginogel, n = 102) or a copper and zinc chelates gel (coppergel, n = 110), for each treatment group

	Day 0		Day 3		Day 7		Day 10	
Treatment group	M-score[1]	N	M-score	N	M-score	N	M-score	N
Alginogel	M1	21	M0	1	M0	1	M2	1
			M1	9	M1	7	M1	6
							M3	1
					M3	1	M4.1	1
					M4	1	M4	1
			M2	3	M2	3	M1	1
							M2	2
			M3	5	M1	1	M4	1
					M3	2	M3	2
					M4	1	M3	1
					M4.1	1	M4.1	1
			M4	3	M4	1	M4.1	1
					M4.1	2	M2	1
							M4.1	1
	M2	72	M1	6	M1	5	M1	3
							M2	1
							M4	1
					M2	1	M2	1
			M2	61	M1	3	M1	2
							M3	1
					M2	58	M1	6
							M2	52
			M3	3	M4	3	M3	1
							M4	2
			M4	2	M2	1	M2	1
					M4	1	M4.1	1

[1]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

Table A4 (Continued). Trimming chute M-score serial transition matrix of active digital dermatitis lesions on hind feet from 171 cows on seven dairy farms between day 0, day 3, day 7, and day 10 following treatment with an enzyme alginogel (alginogel, n = 102) or a copper and zinc chelates gel (coppergel, n = 110), for each treatment group

	Day 0		Day 3		Day 7		Day 10	
Treatment group	M-score[1]	N	M-score	N	M-score	N	M-score	N
Alginogel	M4.1	9	M1	3	M1	2	M0	1
							M1	1
					M2	1	M1	1
			M2	1	M2	1	M2	1
			M3	2	M1	1	M2	1
					M4	1	M3	1
			M4.1	3	M0	1	M0	1
					M4.1	2	M4.1	2
Coppergel	M1	22	M1	2	M1	1	M3	1
					M3	1	M3	1
			M3	18	M3	18	M0	3
							M1	1
							M3	9
							M4	5
			M4	1	M0	1	M0	1
			M4.1	1	M3	1	M3	1

[1]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

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Table A4 (Continued). Trimming chute M-score serial transition matrix of active digital dermatitis lesions on hind feet from 171 cows on seven dairy farms between day 0, day 3, day 7, and day 10 following treatment with an enzyme alginogel (alginogel, n = 102) or a copper and zinc chelates gel (coppergel, n = 110), for each treatment group

	Day 0		Day 3		Day 7		Day 10	
Treatment group	M-score[1]	N	M-score	N	M-score	N	M-score	N
Coppergel	M2	77	M1	10	M1	3	M1	1
							M3	2
					M3	6	M3	6
					M4	1	M0	1
			M2	26	M1	6	M1	2
							M3	4
					M2	12	M1	2
							M2	6
							M3	4
					M3	8	M3	8
			M3	36	M1	2	M3	2
					M2	1	M3	1
					M3	32	M1	1
							M3	30
							M4	1
					M4.1	1	M3	1
			M4.1	5	M3	4	M3	4
					M4.1	1	M3	1
	M4.1	11	M2	2	M4	1	M4	1
					M4.1	1	M3	1
			M3	9	M1	2	M1	1
							M3	1
					M3	7	M3	6
							M4	1

[1]As developed by Döpfer et al. (1997) and extended by Berry et al. (2012).

Table A5. Final reduced multivariable logistic regression analysis results for associations between dichotomous outcome variables, M-score improvement and wound healing progress (with unscorable lesions classified as either "not improved" or "improved") between day 0 and day 10, and different explanatory variables with farm as fixed effect (results not presented) with random selection of one digital dermatitis lesion per cow[1]

	M-score improvement[1]	
Variable	aOR[2]	95% CI
Intercept	2.93	
Treatment group		
Coppergel	1	Referent
Alginogel	0.04	0.01–0.13
Period under bandage		
10 days		
7 days	7.86	2.37–31.42

[1]Data were collected from active digital dermatitis lesions on hind feet from 171 cows on seven dairy farms, treated with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage. M-score improvement was defined as transition to M0-, M3-, or M4-stages or to lesions with a smaller ulcerative area (e.g., M2-stage to M1-stage). With M-stages as developed by Döpfer et al. (1997) and extended by Berry et al. (2012).
[2]Adjusted odds ratio.

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Table A5 (Continued). Final reduced multivariable logistic regression analysis results for associations between dichotomous outcome variables, M-score improvement and wound healing progress (with unscorable lesions classified as either "not improved" or "improved") between day 0 and day 10, and different explanatory variables with farm as fixed effect (results not presented) with random selection of one digital dermatitis lesion per cow[1]

	Wound healing progress[1]			
	Unscorable lesions classified as "not improved"		Unscorable lesions classified as "improved"	
Variable	aOR[2]	95% CI	aOR[2]	95% CI
Intercept	0.11		0.11	
Treatment group				
Coppergel	1	Referent	1	Referent
Alginogel	2.50	0.95–6.61	0.58	0.13–2.82
Period under bandage				
10 days				
7 days			0.12	0.01–0.68
WH0–3[3]				
Not improved				
Improved			7.79	1.74–45.95
WH3–7[4]				
Not improved				
Improved	7.20	2.03–29.17		
WH7–10[5]				
Not improved				
Improved	42.12	9.88–307.42	80.56	19.88–495.99

[1]Data were collected from active digital dermatitis lesions on hind feet from 167 cows on seven dairy farms, treated with an enzyme alginogel or copper and zinc chelates gel (coppergel) with bandage. Lesions with improved wound healing had at least one of the following criteria when compared with the previous observation: decreased defect size, healthier granulation tissue color (pink-red instead of purple-grayish), more regular aspect of granulation tissue surface, wound contraction, or epithelialization starting from the surrounding skin.
[2]Adjusted odds ratio.
[3]Wound healing progress between day 0 and day 3.
[4]Wound healing progress between day 3 and day 7.
[5]Wound healing progress between day 7 and day 10.

Chapter 6

Digital Dermatitis Risk Assessment Questionnaire

Vanhoudt, A., K. Orsel, M. Nielen, and T. van Werven. (2021) An observational study on the management of digital dermatitis through a repeated risk assessment on 19 Dutch dairy herds. J. Dairy Sci. 104: 947–956. doi:10.3168/jds.2020-18730.

ABSTRACT

The etiopathogenesis of bovine digital dermatitis is not well understood, but its risk factors on dairy farms have been studied extensively. The objective of this study was to identify associations between a digital dermatitis risk score (determined by a digital dermatitis risk assessment questionnaire) and digital dermatitis prevalence (determined by an in-parlor M-score). We also investigated whether feedback for farmers on their digital dermatitis management using the digital dermatitis risk assessment questionnaire resulted in changes that decreased digital dermatitis prevalence in their herds. The digital dermatitis risk assessment questionnaire consisted of multiple-choice questions related to foot health, housing, and general management that were used to create a total risk score. In 2016 and 2018, the digital dermatitis risk assessment questionnaire — together with a digital dermatitis prevalence determination in the lactating herd — was used on 19 Dutch dairy farms from one veterinary practice. After each visit, farmers and their consulting veterinarians received a one-page summary that identified herd-specific strengths and weaknesses in digital dermatitis management. In 2018, the summary included suggestions for improvement. In 2019, farmers and veterinarians were contacted to ask whether the use of the digital dermatitis risk assessment questionnaire and the one-page summary had led them to implement changes in their digital dermatitis management in 2016 and 2018. We tested the association between total risk score and digital dermatitis prevalence using linear mixed model analysis. The total risk score ranged from 13 to 65% and 20 to 68% in 2016 and 2018, respectively. Herd digital dermatitis prevalence ranged from 15 to 59% and 27 to 69% in 2016 and 2018, respectively. For both years, the digital dermatitis risk assessment questionnaire identified that days in milk, herd size, and breed were often present in a manner associated with increased risk for digital dermatitis. The linear mixed model analysis identified that each 10-point increase in total risk score was associated with an increase in herd digital dermatitis prevalence of less than 1%. The association between total risk score and herd digital dermatitis prevalence was caused mainly by risk factors related to housing. We found no important relationship between change in total risk score and change in digital dermatitis prevalence between the two

visits. Only a few farmers indicated some form of change in their digital dermatitis management following a visit. Veterinarians in general said that they discussed the one-page summaries and digital dermatitis control with farmers during a routine visit, but the majority admitted a lack of follow-up. We propose that the digital dermatitis risk assessment questionnaire could be used as a tool to start a discussion on digital dermatitis control on farm, but simply undertaking a digital dermatitis risk assessment questionnaire and providing a one-page summary of the results was insufficient to initiate behavioral change that led to a decrease in digital dermatitis prevalence.
Key words: behavioral change, dairy cow, digital dermatitis, questionnaire, risk factor

INTRODUCTION

Following its first description by Cheli and Mortellaro (1974), digital dermatitis quickly became recognized as the most important infectious cause of lameness in dairy cattle. Because certain lesion stages are painful, digital dermatitis has a negative effect on cattle productivity and welfare worldwide (Bruijnis et al., 2012b; Higginson Cutler et al., 2013; Dolecheck and Bewley, 2018).

The etiology of digital dermatitis is probably polybacterial, with lesions consistently containing large numbers of multiple *Treponema* spp. together with a multitude of other bacteria, such as *Dichelobacter nodosus*, *Fusobacterium necrophorum*, *Mycoplasma fermentans*, and *Porphyromonas levii* (Krull et al., 2014; Nielsen et al., 2016; Moreira et al., 2018a). *Treponema* spp. and non-treponema bacterial populations do not appear randomly: they are associated with specific lesion stages and change with lesion progression (Krull et al., 2014; Zinicola et al., 2015b; Beninger et al., 2018). Current treatment and control strategies focus on dealing with this bacterial load, but to date they have been unsuccessful in eradicating the disease from most herds (Yeruham and Perl, 1998). Generally, they result in an endemic balance, with a more or less stable prevalence and the majority of lesions remaining at the chronic M4-stage (Döpfer and Bonino Morlán, 2008; Biemans et al., 2018).

Understanding risk factors and control measures, as reviewed for digital dermatitis by Potterton et al. (2012), Palmer and O'Connell (2015), and Cook (2017), provides valuable insight in the epidemiology of an infectious disease. However, little is known about how to translate this knowledge into an effective digital dermatitis control plan. Two studies from the UK investigated digital dermatitis prevalence reduction as part of a general lameness control program (Bell et al., 2009; Barker et al., 2012), and one Canadian study specifically focused on digital dermatitis prevalence in a controlled footbath intervention program (Solano et al., 2017b). The intervention studies of Bell et al. (2009) and Barker et al. (2012) failed to reduce digital dermatitis prevalence. As important reasons for this outcome, the authors identified poor compliance with advice, a mismatch between the applied communication method and farmer type, and insufficient time to implement changes with significant effect. In contrast, Solano et al., (2017b) achieved a reduction in both active digital dermatitis lesion stages and digital dermatitis prevalence in herds with a high (≥15%) prevalence of active digital dermatitis lesions with a controlled intervention study that implemented best practice foot bathing.

Our study investigates the effect of raising awareness with a digital dermatitis specific risk assessment on the prevalence of digital dermatitis in dairy herds, leaving two years to implement changes with measurable effect. We conducted a repeated cross-sectional field study with a digital dermatitis risk assessment questionnaire and digital dermatitis prevalence determination through in-parlor M-scoring on Dutch dairy farms with routine herd health advice, using each farm as a historical control. The objectives of this study were (1) to identify associations between a digital dermatitis risk score determined by the digital dermatitis risk assessment questionnaire and digital dermatitis prevalence; and (2) to investigate whether feedback on digital dermatitis management through the digital dermatitis risk assessment questionnaire resulted in management changes that decreased digital dermatitis prevalence in herds.

MATERIALS AND METHODS

Ethical Statement

This study was performed in accordance with European law concerning the protection of animals kept for farming purposes (Council Directive 98/58/EC) and was not considered an animal experiment under Dutch legislation. The farmers participated in the research based on an informed consent statement. The veterinarians participated under the teaching agreement between the University Farm Animal Practice and the Faculty of Veterinary Medicine of Utrecht University, all within current Dutch legislation on non-medical research on human subjects.

Data Collection

Herd Selection. In 2016, a convenience sample of 22 herds was selected from the dairy herds (n = 330) served by the University Farm Animal Practice (Harmelen, the Netherlands). The veterinarians from this practice were asked to compile a list of clients that would meet the following selection criteria: a herd with a digital dermatitis problem in the previous months according to the herd's veterinarian; and a milking parlor suitable for in-parlor M-scoring. Farmers from this list were then contacted and asked if they were willing to participate in the study until a total of 22 participants was reached. Of these 22 herds, 19 farmers also agreed to participate in the 2018 digital dermatitis risk assessment questionnaire and farm visit. Dropout reasons were as follows: stopped farming; ongoing transition to organic farming; and did not see the value of participating further in the study. The dairy herd improvement data were extracted from farm-management software with the consent of the participating farmers (pirDAP, the Netherlands).

Digital Dermatitis Risk Assessment Questionnaire. The digital dermatitis risk assessment questionnaire was an interim version of the lameness risk assessment questionnaire developed and validated by the University of Calgary (van Huyssteen et al., 2020). The digital dermatitis risk assessment questionnaire consisted of 22 multiple-choice questions and was composed of sections on foot health, housing, and general herd management (five, eight, and nine questions, respectively; Appendix). Each of the answers to the questions was given a risk score based on the published literature; higher scores indicated a higher risk for digital dermatitis. The risk scores were summed for a total risk score with a maximum of 580; foot health contributed 22%, housing 28%, and general herd management 50%. The digital dermatitis risk assessment questionnaire was conducted during the farm visit by two veterinary students (NH in 2016 and NW in 2018).

Animal-Based Measures. The washed hind feet of the lactating animals were inspected in the milking parlor to score digital dermatitis using the M-score (Döpfer et al., 1997; Relun et al., 2011; Berry et al., 2012; Solano et al., 2017a). During the same milking, the leg hygiene of whichever hind limb was facing the scorer in the milking parlor was also scored (Schreiner and Ruegg, 2002; Cook, 2006; Solano et al., 2015).

Scorer Training. Veterinary students NH and NW were trained by AV in applying the M-score and the leg hygiene score. Training on the M-score was done by a study of the literature, classroom training (39 digital color photographs of cattle feet with varying M-stages provided by KO, 46% agreement between NH and NW), and one in-parlor M-scoring of the washed hind feet of approximately 50 dairy cows together with AV. Leg hygiene score training consisted of studying the score definitions, followed by in-parlor scoring of one lower hind limb of approximately 50 dairy cows under supervision of AV during the in-parlor M-score training.

Farm Visits, Group Meetings, and One-Page Summaries. In February 2016, all farmers (n = 22) and their consulting veterinarians (n = 9) were invited for a meeting on digital dermatitis. The study design and details about data collection methods, together with a brief overview of how to control digital dermatitis on dairy farms, were presented. Farms were then visited once in 2016 and once in 2018—in March or April while the dairy herd was housed. During the farm visit, the scorer went through the digital dermatitis risk assessment questionnaire with the farmer, measured housing parameters (e.g., cubicle type, length, and width), and joined one milking session to perform the in-parlor M-score and leg hygiene score. The sensitivity and specificity of the in-parlor dichotomized M-score compared with scoring of raised feet in the trimming chute were 0.58 to 0.92 and 0.80 to 0.95, respectively (Relun et al., 2011; Solano et al., 2017a; Cramer et al., 2018). We were unable to obtain M-scores on a small number of cows for one or both hind limbs because of their behavior, foot conformation, or the presence of a bandage (n = 82 cows). At the end of the farm visit, farmers were given a list of cows that were scored with an M2-stage lesion and were eligible for treatment. In 2016, one-page summaries were compiled and emailed to the farmer and consulting veterinarian after all farm visits were completed. In 2018, one-page summaries were compiled and emailed to the farmer and consulting veterinarian within 14 days of each farm visit. In July 2018, farmers (19) and veterinarians (10) were again invited for a group meeting, where anonymized results of the study were presented.

Follow-Up Questionnaire. In November 2019, we emailed farmers (n = 19) and their consulting veterinarians (n = 11) from 2016, 2018, or both years and asked them to indicate whether or not the digital dermatitis risk assessment questionnaire and one-page summary had resulted in implementation of changes to their digital dermatitis management in 2016, 2018, or both years. We sent a reminder email in January 2020, and one veterinarian was approached once more to complete the follow-up questionnaire.

Data Handling and Statistical Analyses. Data were collected using pencil and paper, the risk assessment questionnaire, and scoring sheets, and collated into a digital spreadsheet (MS Excel; Microsoft). The 2016 digital dermatitis risk assessment questionnaire and M-score data from the three herds that did not participate in 2018 were excluded from the analyses. Each herd's total risk score was converted to a percentage score by dividing the total risk score by the maximum risk score that could have been achieved from the questions that were answered. The in-parlor M-scores for hind limbs were transformed to a dichotomized (absence and presence) cow-level digital dermatitis prevalence for each herd. Within each herd, M-scores were also grouped into three cow-level digital dermatitis categories: cows without digital dermatitis on both hind feet (**DD-M0**), cows with at least one M2- stage lesion (**DD-M2**), and cows with digital dermatitis but no M2-stage lesion (**DD-other**). Cows with M0 on one hind foot and "unable to score" on the other hind foot, and cows with "unable to score" on both hind feet, were excluded from the analyses (n = 53 cows).

We calculated descriptive statistics for total risk score and herd digital dermatitis prevalence. We tested the association between total risk score (as absolute score divided by 10 for ease of interpretation) and digital dermatitis prevalence (as a percentage) using linear mixed model analyses with (1) total risk score as the predictor and digital dermatitis prevalence measures as the outcome; and (2) total risk score sections (foot health, housing, and general management) as predictors and digital dermatitis prevalence measures as the outcome. In both linear mixed models, we used the year of the digital dermatitis risk assessment questionnaire as a fixed effect and herd as a random effect.

We explored the association between change in total risk score (2018 vs. 2016) as the predictor and change in digital dermatitis prevalence (2018 vs. 2016) as the outcome using a scatter plot to identify the effect of the 2016 digital dermatitis risk assessment questionnaire and one-page summary on digital dermatitis prevalence in 2018. We performed all statistical analyses in SPSS 25.0.0.1 (IBM Corp., New York, NY).

RESULTS

Digital Dermatitis Risk Assessment Questionnaire and Digital Dermatitis Prevalence

An overview of the results of the total risk score and digital dermatitis prevalence for 2016 and 2018 is provided in Figure 6.1. Details for these variables can be found in the Appendix (Table A1). Table 6.1 provides a summary of the answers for a selection of questions from the digital dermatitis risk assessment questionnaire. In 2016, the total risk score varied between 13 and 65% (mean ± standard deviation 42 ± 13%), and herd digital dermatitis prevalence ranged from 15 to 59% (39 ± 14%). In 2018, the total risk score varied between 20 and 68% (41 ± 13%) and herd digital dermatitis prevalence ranged from 27 to 69% (49 ± 10%). Note the high prevalence of cows with M2-stage lesions in herd 17 in 2018 (Figure 6.1b).

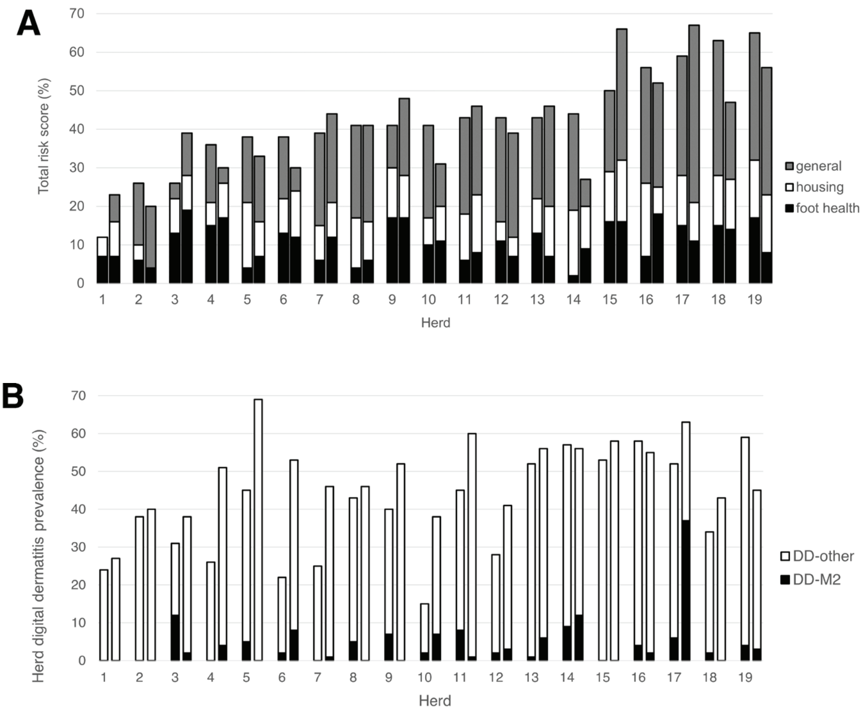

Figure 6.1. An overview of (A) the total risk score and its components as percentage derived from a digital dermatitis risk assessment questionnaire and (B) cow-level herd digital dermatitis prevalence and its composing digital dermatitis categories (DD-M2 for cows with at least one M2-stage lesion and DD-other for cows with digital dermatitis but no M2-stage lesion) from the washed, hind feet, in-parlor M-score (Berry et al., 2012) for 19 Dutch dairy herds visited once in 2016 and once in 2018. Herds are ordered from low to high total risk score in 2016; for each herd, the left bar represents 2016 and the right bar represents 2018.

Table 6.1. Summary of the answers from 19 Dutch dairy herds on a selection of questions from a digital dermatitis risk assessment questionnaire

Question topic (question number)	Risk score	Answer options	Herds (no.)	
			2016	2018
Leg hygiene score (1)	30	>75% score 3–4	2	4
	20	>75% score 2–3	7	15
	10	>75% score 1–2	10	0
Foot trimming schedule[1] (2)	30	Only lame cows	6	6
	20	Cows at dry-off	3	4
	0	Routine at dry-off and 100 days in milk	3	2
	0	Routine whole herd	9	11
Foot bathing schedule (5)	40	No foot bathing	10	8
	30	Interval >4 weeks	0	1
	15	Every 4 weeks	2	2
	0	Every 2 weeks	7	8
Flooring type[2] (9)	10	Slatted floor	18	17
Manure scraping method[2] (10)	30	No manure scraping	3	1
	10	Manual manure scraping	2	5
	0	Automatic manure scraping	6	3
	0	Robotic scraping	8	9

[1]More than one answer possible; lowest risk score was used when multiple answer options were given.
[2]The answer for one or more herds was missing.
[3]Additional information gathered during the farm visit. NA = not applicable.

Table 6.1 (Continued). Summary of the answers from 19 Dutch dairy herds on a selection of questions from a digital dermatitis risk assessment questionnaire

Question topic (question number)	Risk score	Answer options	Herds (no.)	
			2016	2018
Breed of the lactating herd (15)	50	>85% was 100% Holstein-Friesian	11	13
	0	≤85% was 100% Holstein-Friesian	8	6
Purchase of cattle (18)	40	>10% of lactating herd during the previous 12 months	3	1
	10	1–5% of lactating herd during the previous 12 months	1	1
	0	No purchase during the previous 12 months	15	17
Cubicle bedding type[3]	NA	Rubber mat with <2 cm top dressing	10	10
	NA	Cow mattress with <2 cm top dressing	3	3
	NA	Concrete with >2 cm top dressing	2	2
	NA	Waterbed with <2 cm top dressing	2	2
	NA	Half concrete, half rubber, both with <2 cm top dressing	1	1
	NA	Recycled manure solids with a depth >2 cm	1	1

[1]More than one answer possible; lowest risk score was used when multiple answer options were given.
[2]The answer for one or more herds was missing.
[3]Additional information gathered during the farm visit. NA = not applicable.

Linear mixed model analysis identified that herd digital dermatitis prevalence was approximately 10% higher in 2018 than in 2016 (95% CI 4.51 to 16.29; Table 6.2). Using total risk score and digital dermatitis data from both digital dermatitis risk assessment questionnaire years, we found that each 10-point increase in total risk score was associated with an increase in herd digital dermatitis prevalence of less than 1% (0.63, 95% CI 0.05 to 1.22). This association disappeared for the prevalence of DD-M2 cows, but remained a trend for the prevalence of DD-other cows (0.59, 95% CI –0.007 to 1.18). Linear mixed model analysis with total risk score section scores indicated that the section score for housing had the most influence on the digital dermatitis prevalence outcomes relative to the section scores for foot health and general management (Table 6.3).

In the herds with lowest herd digital dermatitis prevalence, manure scraping was automatic or robotic; cows had at least eight hours access to pasture during the grazing season with a cow track of at least 150 m; the lactating herd size was less than 90 cows; and a maximum 85% of the lactating herd was 100% Holstein-Friesian. These responses all had a risk score of zero on the risk assessment questionnaire. In the herds with the highest herd digital dermatitis prevalence, more than 85% of the lactating herd was 100% Holstein-Friesian; 80% or more of the lactating herd was more than 60 days in milk; and the lactating herd size was 90 cows or more. These responses all had a maximum risk score on the risk assesment questionnaire.

The changes in total risk score and herd digital dermatitis prevalence from 2018 to 2016 are visualized in Figure 6.2. In four herds, both total risk score and herd digital dermatitis prevalence increased at least 5%, and in four herds total risk score decreased at least 5% and herd digital dermatitis prevalence increased at least 5%. In these eight herds, changes in total risk score originated from changes in the general management section. In herd 19, both total risk score and herd digital dermatitis prevalence decreased at least 5%. The scatter plot demonstrates that we found no important relationship between the change in total risk score (2018 vs. 2016) as the predictor and the change in digital dermatitis prevalence (2018 vs. 2016) as the outcome (Figure 6.3).

Table 6.2. Results from linear mixed model analyses testing the association between total risk score and digital dermatitis prevalence in 19 Dutch dairy herds visited once in 2016 and once in 2018[1]

		95% Confidence interval	
Item	Estimate	Lower	Upper
Herd digital dermatitis prevalence			
Intercept	35.28	21.31	49.25
Total risk score	0.63	0.05	1.22
2018 vs. 2016	10.40	4.51	16.29
DD-M2[2] prevalence			
Intercept	1.74	–6.25	9.72
Total risk score	0.13	–0.21	0.46
2018 vs. 2016	0.97	–3.24	5.19
DD-other[3] prevalence			
Intercept	31.79	17.62	45.96
Total risk score	0.59	–0.007	1.18
2018 vs. 2016	9.48	2.94	16.01

[1]Total risk score is expressed as absolute score divided by 10; digital dermatitis prevalence is expressed as percentage; year of the questionnaire was a fixed effect, and herd was a random effect.
[2]Cows with at least one M2-stage lesion from a washed, hind feet, in-parlor M-score (Berry et al., 2012).
[3]Cows with digital dermatitis but no M2-stage lesion from a washed, hind feet, in-parlor M-score.

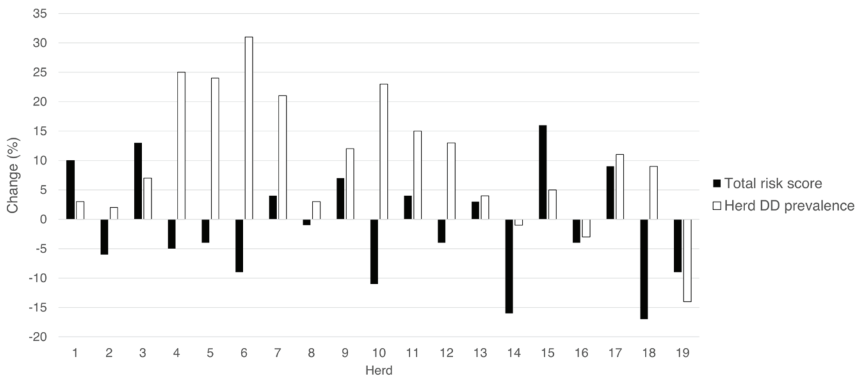

Figure 6.2. Changes (2018 to 2016) in total risk score (as a percentage) and cow-level herd digital dermatitis (DD) prevalence following a digital dermatitis risk assessment questionnaire and associated one-page summary for 19 Dutch dairy herds visited once in 2016 and once in 2018. Herds are ordered from low to high total risk score in 2016.

Table 6.3. Results from linear mixed model analyses testing the association between total risk score sections and digital dermatitis prevalence in 19 Dutch dairy herds visited once in 2016 and once in 2018[1]

		95% Confidence interval	
Item	Estimate	Lower	Upper
Herd digital dermatitis prevalence			
Intercept	30.59	16.04	45.13
Foot health	0.18	–1.21	1.56
Housing	2.68	0.94	4.42
General management	0.28	–0.43	0.99
2018 vs. 2016	11.23	5.20	17.26
DD-M2[2] prevalence			
Intercept	3.15	–6.06	12.35
Foot health	–0.29	–1.19	0.61
Housing	0.20	–0.94	1.35
General management	0.19	–0.28	0.65
2018 vs. 2016	1.20	–3.03	5.42
DD-other[3] prevalence			
Intercept	26.82	11.56	42.09
Foot health	0.45	–1.01	1.92
Housing	2.53	0.69	4.38
General management	0.13	–0.62	0.89
2018 vs. 2016	10.08	3.48	16.68

[1]Total risk score is expressed as absolute score divided by 10; digital dermatitis prevalence is expressed as percentage; year of the questionnaire was a fixed effect, and herd was a random effect.
[2]Cows with at least one M2-stage lesion from a washed, hind feet, in-parlor M-score (Berry et al., 2012).
[3]Cows with digital dermatitis but no M2-stage lesion from a washed, hind feet, in-parlor M-score.

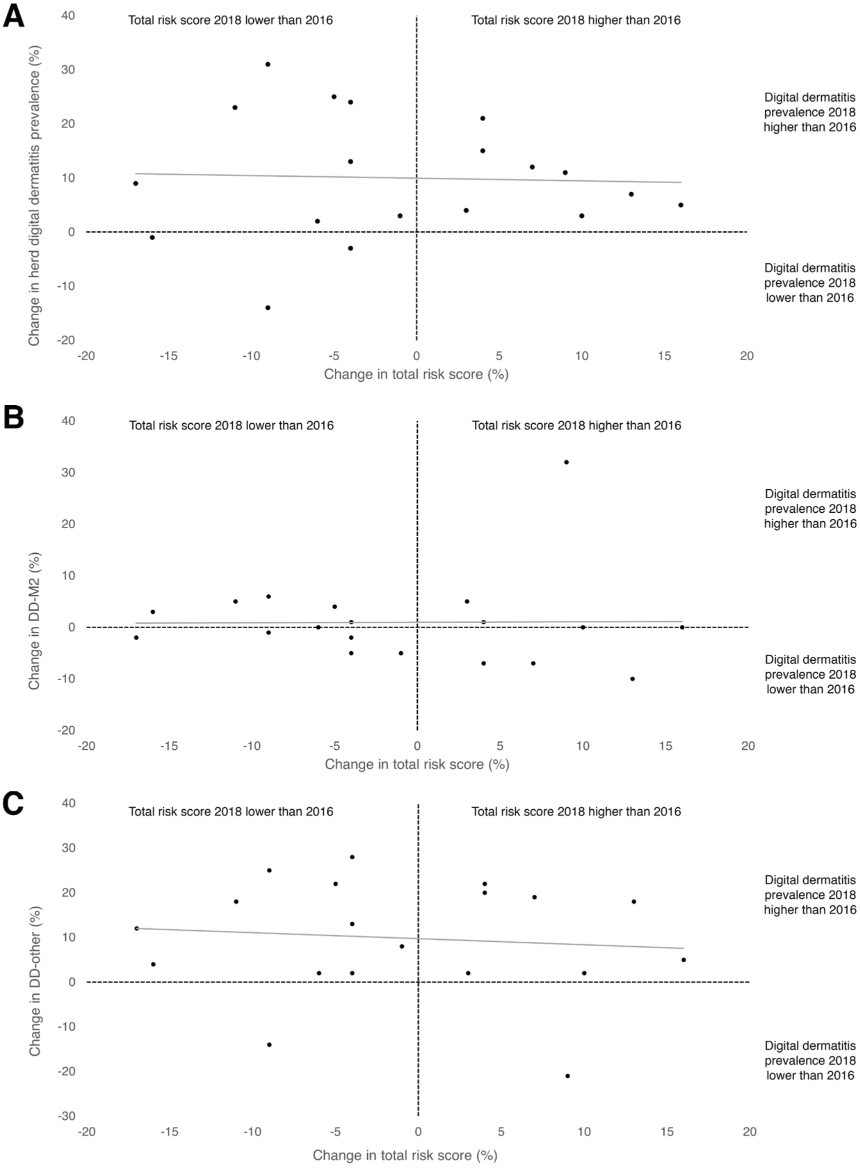

Figure 6.3. Scatter plot with a solid linear trend line visualizing the association between the difference (2018 to 2016) in total risk score as a predictor and the difference in (A) cow-level herd digital dermatitis prevalence, (B) the prevalence of cows with at least one M2-stage lesion (DD-M2), and (C) the prevalence of cows with digital dermatitis but no M2-stage lesion (DD-other) as outcomes for 19 Dutch dairy herds visited once in 2016 and once in 2018.

One-Page Summaries

In 2016 and 2018, one-page summaries described overall findings from the study and provided farm-specific risk factors. In 2018, the summaries also provided suggestions for enhancement of the herd's digital dermatitis management. For both years, the digital dermatitis risk assessment questionnaire identified that days in milk, lactating herd size, and breed were often present in a manner associated with increased risk for digital dermatitis, and that few herds purchased cattle. "Improve overall hygiene and leg hygiene" was most frequently suggested to ameliorate digital dermatitis management, followed by "Introduce breeds known to be less susceptible to digital dermatitis" (18 and 12 times, respectively). "Disinfect foot trimming equipment" and "Implement a footbath" were other frequent suggestions (7 and 5 times, respectively).

Follow-Up Questionnaire

The response rate for the follow-up questionnaire was 53% for farmers and 100% for veterinarians. Four farmers indicated some form of change in their digital dermatitis management in 2016, and seven farmers indicated change in 2018. Increasing the foot bathing regimen, ensuring prompt treatment of affected cows, and improving hygiene through manure scraping and disinfection of foot trimming equipment were changes made. In general, veterinarians said that they discussed the one-page summaries and digital dermatitis control with the farmer during a routine visit, but the majority admitted lack of follow-up.

DISCUSSION

We identified a small association between a higher total risk score and a higher herd digital dermatitis prevalence. This association was mainly explained by risk factors in the housing section of the risk assement questionnaire (all related to exposure to infectious fecal material) rather than by risk factors in the foot health section. This may be because foot trimming practices are related to foot health in general, instead of specific to digital dermatitis prevalence. It could also be that foot bathing practices used by the herds in our study did not comply with what is currently considered to be best practice (Cook, 2017; Solano et al., 2017b). Unfortunately, details about foot bathing practices were not included in the digital dermatitis risk assessment questionnaire. The small association we observed between total risk score and herd digital dermatitis prevalence did not seem driven by the small proportion of cows with M2-stage lesions, but rather by the majority of cows with other M-stage lesions, mostly M4-stage. Because cows with M4-stage lesions play an important role in the digital dermatitis transmission dynamics in a herd, total risk score combined with herd digital dermatitis prevalence can be used to identify herd-specific improvement opportunities for digital dermatitis control.

We identified a higher herd digital dermatitis prevalence in 2018 than in 2016. A similar trend in digital dermatitis prevalence was seen in the voluntary national Dutch database of foot trimming records [personal communication, Pieter van Goor (Arnhem, the Netherlands); DigiKlauw, CRV (Arnhem, the Netherlands) and Royal GD (Deventer, the Netherlands)]. A possible explanation for the lack of decrease in herd digital dermatitis prevalence as a consequence of the digital dermatitis risk assessment questionnaire is the study design. The one-page summaries identified herd-specific risk factors for digital dermatitis and contained non-committal improvement options for digital dermatitis management. Whether or not these items were addressed relied on the farmers and their consulting veterinarians. The majority of veterinarians in our study discussed the one-page summaries with their clients but did not follow-up after the initial discussion. A recent intervention study on foot bathing regimens reported that implementation of best practice foot bathing by researchers resulted in improved control of digital dermatitis on dairy farms with a high (≥15%)

prevalence of active digital dermatitis lesions (Solano et al., 2017b).

The selection criterion "willingness to participate in the study" probably resulted in the selection of more progressive farmers who likely perceived digital dermatitis as a problem in their herd and were eager to learn about the disease and how to control it. Still, only four of 10 farmers who answered the follow-up questionnaire changed their digital dermatitis management in 2016. Unfortunately, none of the farmers in our study explained why they did not change their digital dermatitis management. One veterinarian indicated that farmers had ample reasons for not implementing advice when they were asked why they did not make changes. Relun et al. (2013a) state that the main barriers for French dairy farmers in adopting individual or collective digital dermatitis treatments were required time and labor, followed by costs. Likewise, Bruijnis et al. (2013) identified labor efficiency and a long wait before seeing an improvement as possible barriers, and cost-effective measures as the main driver for achieving better foot health in a study with Dutch dairy farmers. Insufficient time to implement recommended changes that had a significant effect on foot health was one of the reasons for failure of the lameness control plan for heifers in dairy farms from the UK (Bell et al., 2009). Similar barriers to implementing changes or control strategies were also identified for Johne's disease (Roche et al., 2019). We refer the readers to the review by Ritter et al. (2017) for more information on the sociophysiological drivers for adoption of management strategies for infectious diseases by farmers.

The risk score for the questions in the digital dermatitis risk assessment questionnaire used in this study ranged from zero (low) to 60 (high) risk points, but in the lameness risk assesment questionnaire eventually developed by the University of Calgary (van Huyssteen et al., 2020), each question was given a risk score of zero (low) to three (high). Both approaches resulted in systematic identification of areas and farms at high risk for digital dermatitis based on the best knowledge available at the time of developing the risk assessment questionnaire. The digital dermatitis risk assessment questionnaire can be used to monitor trends and allows for benchmarking within and between herds. The most likely application of the digital dermatitis risk assessment questionnaire would be to help advisors raise awareness of the current risk for digital dermatitis in a given herd. Incorporating risk factors such as days in milk, herd size, and predominant breed can still be useful for identifying risk intensity, allowing the farmers to tailor their overall digital dermatitis control management even though the specific risks cannot be managed. By applying a semi-qualitative tool such as the digital dermatitis risk assessment questionnaire, interviewers can approach the topic with respect for the attitudes and beliefs of the respondents, who are encouraged to take part in the discussion and indicate what they feel is important (Braun and Clarke, 2013).

Two veterinary students collected the data for this study. Although they were both trained equally, observer bias may have occurred between 2016 and 2018 for farm characteristics and for M-scores. We found moderate agreement between the two students for M-scores. With dichotomization of the M-score into the presence or absence of digital dermatitis, which has almost perfect interobserver agreement (Vanhoudt et al., 2019), we likely kept the effect of this bias to a minimum.

We ascertained no important relationship between the change in total risk score and the change in digital dermatitis prevalence. Most current digital dermatitis treatment and control measures are aimed at transition to or maintenance at the manageable M4-stage (Döpfer and Bonino Morlán, 2008). Because the M4-stage is the most important driver for transmission of digital dermatitis (Biemans et al., 2018), it is a probable explanation for the lack of an association between the change in total risk score and the change in digital dermatitis prevalence in our study. Within each herd, the prevalence of digital dermatitis remains relatively stable and appears to vary around an endemic balance. With current digital dermatitis management focused mainly on maintaining relatively low levels of the often painful M2-stage lesions by early detection and prompt treatment, the welfare of affected cows is looked after; however, transmission of the disease through M4-stage lesions continues, leading to a herd-specific endemic balance. We therefore suggest that all stages of digital dermatitis, like all affected production groups, be considered in the management of digital dermatitis when aspiring to reduce digital dermatitis prevalence.

CONCLUSIONS

The digital dermatitis risk assessment questionnaire can be used to identify herd-specific risk factors for digital dermatitis and raise awareness of strong and weak points for digital dermatitis control on dairy farms. However, as a standalone intervention the digital dermatitis risk assessment questionnaire is insufficient to initiate behavioral change from farmers and their consulting veterinarians that results in a decrease in digital dermatitis prevalence under field conditions. Identifying drivers for the adoption of digital dermatitis management strategies by farmers, together with an integrated approach that deals with all stages of digital dermatitis in all affected production groups, is needed for a decrease in digital dermatitis prevalence and improved control of the disease.

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COMPETING INTERESTS

All authors declare that they have no conflict of interest related to the study discussed in this manuscript.

APPENDIX

Digital Dermatitis Risk Assessment Questionnaire

Foot Health Section	**Risk Score**
1. Leg hygiene score, as described by Solano et al. (2015)	
a. ≥75% of the cows scored 3–4	30
b. ≥75% of the cows scored 2–3	20
c. ≥75% of the cows scored 1–2	10
d. ≥75% of the cows scored 1	0
In-parlor score of one lower hind limb per cow (whichever hind limb was facing the scorer in the milking parlor).	
2. What is your foot trimming schedule? More answers possible.	
a. Cows are never trimmed	40
b. Only lame cows are trimmed	30
c. Heifers are trimmed before introduction into the lactating herd	30
d. Cows are trimmed at dry-off	20
e. Routine trim at dry-off and around 100 days in milk	0
f. Routine whole herd trim	0
If the answer is a.–e., skip Q3. If the answer is f., please answer Q3.	
3. When was the last routine whole herd trim?	
a. >7 months ago	20
b. 5.5–7 months ago	10
c. <5.5 months ago	0
4. Does your foot trimmer disinfect his equipment before trimming?	
a. No	20
b. Yes	0
5. How often do your cows walk through a footbath?	
a. I do not use a footbath	40
b. At an interval longer than 4 weeks	30
c. Once per month	15
d. Once per fortnight	0

Housing Section	**Risk Score**
6. Average cubicle length	
a. <2.30 meters	20
b. ≥2.30 meters	0
Measured distance between the hind curb of the cubicle and the front end of the cubicle for single row cubicles or the center of the lunging area for double row cubicles from 3 to 4 cubicles.	
7. Average cubicle width	
a. <1.15 meters	20
b. ≥1.15 meters	0
Measured distance between the center of the left and the center of the right cubicle separator from 3 to 4 cubicles.	
8. Cubicle separator type	
a. Legless	20
b. R-type	10
c. English	0
9. Flooring type	
a. Grooved solid concrete floor	30
b. Non-grooved solid concrete floor	20
c. Slatted floor	10
d. Straw yard	0
If the answer is a.–c., please answer Q10. If the answer is d., skip Q10.	
10. How do you scrape the manure of your floor?	
a. No manure scraping	30
b. Manual manure scraping	10
c. Automatic manure scraping	0
d. Robotic manure scraping	0
If the answer is a. or d., skip Q11. If the answer is b. or c., please answer Q11.	
11. What is the frequency of manure scraping?	
a. <3 times per day	20
b. 3–6 times per day	10
c. >6 times per day	0

Housing Section (Continued)	Risk Score
12. Do your cows have access to pasture during the grazing season?	
a. No access to pasture	40
b. <8 hours per day	20
c. ≥8 hours per day	0
If the answer is a., skip Q13. If the answer is b. or c., please answer Q13.	
13. How long is the cow track to the pasture?	
a. <150 meters	20
b. ≥150 meters	0
General Herd Management Section	
14. What is the size of the lactating herd?	
a. ≥90 animals	20
b. <90 animals	0
15. Percentage of lactating herd that is 100% Holstein-Friesian:	
a. >85%	50
b. ≤85%	0
16. Percentage of the herd that has parity 3 or more:	
a. <40%	60
b. ≥40%	0
17. Percentage of the herd that is more than 60 days in milk:	
a. ≥80%	40
b. <80%	0
18. Did you purchase cattle during the previous 12 months?	
a. >10% of the lactating herd	40
b. 6–10% of the lactating herd	20
c. 1–5% of the lactating herd	10
d. No	0
If the answer is a.–c., please answer Q19. If the answer is d., skip Q19.	
19. Which type of cattle did you purchase?	
a. Heifer	20
b. Cow	10

General Herd Management Section (Continued)	Risk Score
20. From what age are youngstock housed in the same building as dairy cows (sharing airspace but no direct contact)?	
a. Youngstock is not housed in the same building as dairy cows	20
b. From >1 year of age	10
c. From ≤1 year of age	0
21. When are dry cows returned into the lactating herd?	
a. >14 days before the calculated calving date	20
b. 1–14 days before the calculated calving date	10
c. After calving	0
22. Over what time period do you reach maximum concentrate gift after calving?	
a. ≤2 weeks	20
b. >2 weeks	0

Table A1. Overview of the total risk score and its components from a digital dermatitis risk assessment questionnaire and cow level digital dermatitis prevalence from washed hind feet in-parlor M-scores (Berry et al., 2012) from 19 Dutch dairy herds visited once both in 2016 and 2018; herds are ordered from low to high total risk score in 2016

				Digital dermatitis risk assessment questionnaire				
Herd	Year	N[1]	Total risk score[2] (%)	% Foot health	% Housing	% General herd management	Digital dermatitis[3] (%)	% M2[4]
1	2016	66	70/560 (13)	7	5	0	16/66 (24)	0
	2018	65	130/560 (23)	7	9	7	17/64 (27)	0
2	2016	128	115/450 (26)	6	4	16	49/128 (38)	0
	2018	114	100/510 (20)	4	0	16	43/113 (40)	0
3	2016	60	140/540 (26)	13	9	4	18/59 (31)	12
	2018	55	210/540 (39)	19	9	11	21/55 (38)	2
4	2016	62	190/540 (35)	15	6	15	16/62 (26)	0
	2018	57	160/540 (30)	17	9	4	29/57 (51)	4
5	2016	66	200/540 (37)	4	17	17	30/66 (45)	5
	2018	61	180/540 (33)	7	9	17	41/61 (69)	0
6	2016	42	210/560 (38)	13	9	16	9/41 (22)	2
	2018	49	150/520 (29)	12	12	6	26/49 (53)	8
7	2016	115	215/540 (40)	6	9	24	27/113 (25)	0
	2018	103	245/560 (44)	12	9	23	44/102 (46)	1

[1]Number of cows scored in the milking parlor.
[2]Total risk score out of maximal risk score.
[3]Cow level digital dermatitis (DD) prevalence in the herd excluding cows unable to be classified in a DD category using their hind feet M-scores.
[4]Percentage of cows with at least one M2 stage lesion on their hind feet .

Table A1 (Continued). Overview of the total risk score and its components from a digital dermatitis risk assessment questionnaire and cow level digital dermatitis prevalence from washed hind feet in-parlor M-scores (Berry et al., 2012) from 19 Dutch dairy herds visited once both in 2016 and 2018; herds are ordered from low to high total risk score in 2016

				Digital dermatitis risk assessment questionnaire				
Herd	Year	N[1]	Total risk score[2] (%)	% Foot health	% Housing	% General herd management	Digital dermatitis[3] (%)	% M2[4]
8	2016	105	220/540 (41)	4	13	24	45/104 (43)	5
	2018	100	210/520 (40)	6	10	25	46/100 (46)	0
9	2016	126	220/540 (41)	17	13	11	50/126 (40)	7
	2018	114	260/540 (48)	17	11	20	58/112 (52)	0
10	2016	60	240/580 (41)	10	7	24	9/60 (15)	2
	2018	73	170/560 (30)	11	9	11	28/73 (38)	7
11	2016	121	220/520 (42)	6	12	25	52/118 (45)	8
	2018	123	240/520 (46)	8	15	23	69/119 (60)	1
12	2016	185	240/560 (43)	11	5	27	51/185 (28)	2
	2018	189	220/560 (39)	7	5	27	77/188 (41)	3
13	2016	137	240/560 (43)	13	9	21	66/134 (52)	1
	2018	133	250/540 (46)	7	13	26	68/126 (56)	6
14	2016	99	230/520 (44)	2	17	25	56/99 (57)	9
	2018	89	150/540 (28)	9	11	7	48/89 (56)	12

[1]Number of cows scored in the milking parlor.
[2]Total risk score out of maximal risk score.
[3]Cow level digital dermatitis (DD) prevalence in the herd excluding cows unable to be classified in a DD category using their hind feet M-scores.
[4]Percentage of cows with at least one M2 stage lesion on their hind feet .

Table A1 (Continued). Overview of the total risk score and its components from a digital dermatitis risk assessment questionnaire and cow level digital dermatitis prevalence from washed hind feet in-parlor M-scores (Berry et al., 2012) from 19 Dutch dairy herds visited once both in 2016 and 2018; herds are ordered from low to high total risk score in 2016

				Digital dermatitis risk assessment questionnaire				
Herd	Year	N[1]	Total risk score[2] (%)	% Foot health	% Housing	% General herd management	Digital dermatitis[3] (%)	% M2[4]
15	2016	66	280/560 (50)	16	13	21	35/66 (53)	0
	2018	69	370/560 (66)	16	16	34	38/69 (58)	0
16	2016	141	300/540 (56)	7	19	30	82/141 (58)	4
	2018	132	290/560 (52)	18	7	27	68/128 (55)	2
17	2016	89	320/540 (59)	15	13	31	45/86 (52)	6
	2018	92	325/480 (68)	11	10	46	51/83 (63)	37
18	2016	94	340/540 (63)	15	13	35	31/92 (34)	2
	2018	90	260/560 (46)	14	13	20	37/86 (43)	0
19	2016	140	340/520 (65)	17	15	33	83/140 (59)	4
	2018	134	290/520 (56)	8	15	33	54/131 (45)	3

[1]Number of cows scored in the milking parlor.
[2]Total risk score out of maximal risk score.
[3]Cow level digital dermatitis (DD) prevalence in the herd excluding cows unable to be classified in a DD category using their hind feet M-scores.
[4]Percentage of cows with at least one M2 stage lesion on their hind feet .

If knowledge is power,

then knowing what we don’t know is wisdom.

Adam Grant

Chapter 7

General Discussion

This chapter reviews the insights gained on the research presented in this thesis with suggestions for future research on three aspects of managing digital dermatitis in dairy herds: (1) detection of feet with digital dermatitis, (2) treatment of digital dermatitis, and (3) herd-level control of digital dermatitis. Finally an approach to substantially reduce the prevalence of digital dermatitis in a dairy herd is suggested.

DETECTION OF FEET WITH DIGITAL DERMATITIS

The inspection of washed feet lifted in a trimming chute, including visualization of the interdigital cleft is considered best practice, but is laborsome. As an alternative, screening methods with inspection of feet from cows standing in the milking parlor, at a management rail, or in their pen were developed (Relun et al., 2011; Solano et al., 2017a; Cramer et al., 2018). These alternative screening methods have been tested on washed and unwashed feet and use the aid of a bright light, a mirror, an infrared thermography camera, computer vision and artificial intelligence, or a combination of these (Relun et al., 2011; Stokes et al., 2012b; Solano et al., 2017a; Cramer et al., 2018; Cernek et al., 2020). In this thesis, the use of maximum infrared thermography temperature for on-farm detection of feet with a digital dermatitis lesion was investigated (Chapter 4; Vanhoudt et al., 2023). Automated identification of feet affected by digital dermatitis using infrared thermography was considered unlikely due to the poor associations between maximum temperature of the plantar pastern region and the presence of an M2 lesion or any digital dermatitis lesion. Other studies report a higher maximum infrared thermography temperature of feet with digital dermatitis when compared with feet without digital dermatitis (Stokes et al., 2012b; Alsaaod et al., 2014; Anagnostopoulos et al., 2021a), yet maximum infrared thermography temperature does not differentiate feet with digital dermatitis from feet with other lesions (Stokes et al., 2012b; Alsaaod et al., 2014).

All the above mentioned alternative screening methods have in common that they result in a considerable proportion of feet with digital dermatitis lesions being missed (hereafter ‘false negatives’) and too many feet without digital dermatitis lesions being flagged for the farmer (hereafter ‘false positives’). Too many false negatives are unwanted as these animals warrant treatment, whereas too many false positives are unwanted due to the amount of effort the farmer has to put in to check the feet in the trimming chute. Another possible unwanted aspect of too many false positives is irresponsible use of antimicrobials when animals are treated without confirmation of the diagnosis. Possible reasons for false negative results are the anatomical location of the digital dermatitis lesion, e.g. in the interdigital cleft, small size of the lesion, low heel height of the claws, and presence of fecal contamination. Whereas possible reasons for false positive results are unreliable identification of the M2-stage by the observer (Chapter 3; Vanhoudt et al., 2019) and the presence of other lesions or infections of the foot.

With the majority of foot lesions that cause lameness requiring treatment in the trimming chute, one could argue that instead of detecting specific lesions, the early identification of feet with compromised foot health, regardless of lesion type, should be the aim of detection. The follow-up for these feet in the trimming chute for diagnosis and lesion specific treatment, remains labor-intensive but would focus on cows with compromised foot health. Detection and treatment of lesions at the early, ideally subclinical, stage limits their impact on production and welfare, and increases their likelihood to cure (Groenevelt et al., 2014). This would help farmers to improve the foot health, productivity, and animal welfare on their farms.

To date, several technologies have been tested to identify feet with compromised foot health, e.g. infrared thermography for digital dermatitis, lesions other than digital dermatitis, and lameness (Alsaaod and Büscher, 2012; Main et al., 2012; Stokes et al., 2012b; Alsaaod et al., 2014; Wood et al., 2015; Werema et al., 2021); computer vision and machine learning for digital dermatitis and lameness (Cernek et al., 2020; Anagnostopoulos et al., 2021b); and metabolomics and kinetic and kinematic methods for lameness (Alsaaod et al., 2017; Weiss et al., 2017; Oehme et al., 2019; O’Leary et al., 2020; Tijssen, 2021; He et al., 2022). However, each technology comes with limitations and the optimal technology for early detection of feet with compromised foot health is still to be established. Compared with automated mastitis and estrus detection (Reith and Hoy, 2018; Steele et al., 2020), it appears probable that integration of multiple technologies with on-farm data on production and cow behavior could make the automated detection of feet with compromised foot health possible (Van Nuffel et al., 2015; Bell and Walker, 2016; Alsaaod et al., 2019). The use of repeated measures and algorithms, allowing comparison within cow and herd, should be able to result in highly sensitive and specific detection of feet with compromised foot health, and this should be explored in future research.

TREATMENT OF LESIONS OF DIGITAL DERMATITIS

Current treatment strategies focus on dealing with the clinical consequences of active lesions. Most commonly studied topical treatment products are tetracyclines, copper and zinc chelates, and salicylic acid. Following topical treatment with the majority of products, a substantial number of treated lesions progress into chronic lesions (Schultz and Capion, 2013; Klawitter et al., 2019). Studies with longer follow-up periods also indicate a recurrence rate to active lesions in up to 50% of treated lesions (Berry et al., 2012; Gomez et al., 2015; Krull et al., 2016b).

In Chapter 5 the application of wound management principles to digital dermatitis lesions was explored. In this study, digital dermatitis lesions were considered infected wounds that heal by second-intention (Vanhoudt et al., 2022). General principles of wound management for second-intention wound healing require the application of a bandage (Elce, 2017). Bandages allow sufficient contact time by keeping treatment products in place and absorb wound exudate while maintaining a humid wound environment. They also offer protection from external factors such as temperature, trauma, and bacterial contamination. On the other hand, managing bandages can be challenging in a wet environment such as pasture-based systems or herds frequently using footbaths. Although there still is much debate concerning the use of bandages in topical treatment of digital dermatitis, mainly driven by the fear of bandage injuries when they stay on too long, current evidence is in favor of bandages. Those studies achieving the highest cure rates to M0 (>85%) all have the application of a bandage incorporated in the treatment protocol, with most of them keeping the bandage on for at least seven days and up to 28 days with weekly reapplication (Capion et al., 2018; Klawitter et al., 2019; El-Shafaey et al., 2021; Sellera et al., 2021; Alsaaod et al., 2022). Only two studies compared the effect of adding a bandage to a specific topical treatment product. Adding a waterproof bandage to a treatment protocol with a chlortetracycline spray or copper and zinc chelates gel, more or less doubled cumulative cure rates to M0 at 28 days (Klawitter et al., 2019). Adding a bandage for 48h to a topical treatment with tetracycline paste led to a non-significant 10% higher cure rate to M0 at eight to 12 days (Higginson Cutler et al., 2013). Further studies are needed to elucidate the role of bandages in the treatment of digital dermatitis lesions.

The outcome of successful wound management is the return to unaffected skin or a functional scar. A limited number of topical treatment protocols manage to achieve high levels (≥80%) of lesion progression to unaffected skin, i.e. the M0-stage (Klawitter et al., 2019; El-Shafaey et al., 2021; Sellera et al., 2021; Alsaaod et al., 2022). The treatment protocol in these studies is characterized by repeated topical application of an antimicrobial component, mostly a wound dressing, and a bandage. In general bandages were kept in place for a week and high cumulative cure rates to M0 were achieved after four treatments including bandage renewal. However, most topical treatment protocols result in the majority of lesions progressing to the chronic M4-stage. Little is known about why the wound healing of these lesions arrests in the chronic stage and what the role is of current treatment practices in the development of chronic lesions. This is in shrill contrast to the wealth of research and knowledge on wound healing in other species such as horses, dogs, cats, and humans. Future research should look to improve our understanding of wound healing in cattle and its application in the treatment of digital dermatitis to enable the majority of digital dermatitis lesions to progress to unaffected skin.

Although little is known about the role of encysted *Treponema* spp. in disease transmission and recurrence of lesions, aiming for full bacteriological cure seems legitimate given the importance of *Treponema* spp. in the etiology of digital dermatitis. Few topical treatment protocol studies also investigated bacteriological cure rates, with reported values for absence of spirochetes on histopathological evaluation of biopsies ranging between 15 and 100% (Berry et al., 2012; Capion et al., 2018; Yamamoto et al., 2018; Sellera et al., 2021; Alsaaod et al., 2022). Despite that taking biopsies to evaluate bacteriological cure interferes with the lesion, future treatment trials should incorporate this in the study protocol.

In conclusion, while current treatment strategies in general succeed to resolve the pain and production losses associated with active lesions of digital dermatitis, too many lesions remain chronic with a high recurrence rate to active lesions. Hereby the disease remains endemic in the herd. In order to progress the control of digital dermatitis toward reduction of prevalence and ultimately eradication from a herd, chronic lesions should not be tolerated and the aim for treatment protocols should be a return to unaffected skin together with bacteriological cure.

CONTROL OF DIGITAL DERMATITIS AT HERD LEVEL

Current control strategies of digital dermatitis result in an endemic equilibrium in which we treat active lesions, mainly M2, and aim to prevent new infections through management practices such as footbathing. In the meantime, we tolerate relatively high levels of chronic lesions, mainly M4. Considering that digital dermatitis is a highly infectious disease, control measures resulting in an endemic equilibrium with >20% chronic infected animals are insufficient for effective disease control. Effective control strategies for digital dermatitis should aim at reducing the prevalence of infected animals, with currently the best dairy herds achieving a prevalence of any digital dermatitis lesion below 10% (Bell and Vanhoudt, 2020). Following general principles of infectious disease control, this can be achieved by reducing the number of infectious animals, reducing disease transmission, and decreasing the susceptibility of the host.

Reducing the Number of Infectious Animals

With *Treponema* spp. identified in all lesion stages of digital dermatitis (Brodard et al., 2021), all animals with any lesion of digital dermatitis should be considered infectious. Hence, all lesions of digital dermatitis, regardless of lesion stage, warrant treatment. In practice, this comes down to including chronic stages in treatment protocols. Some studies also reported treatment outcomes for chronic lesions with overall lower cure rates to unaffected skin when compared with treatment outcomes for active lesions (Kofler et al., 2015; Capion et al., 2018). Like for active lesions, the treatment of chronic lesions should also aim at achieving high levels of return to unaffected skin and bacteriological cure. Potential candidates for topical treatment that need studying are antimicrobial wound dressings used for second-intention healing of similar lesions, ideally involving *Treponema* spp., in other species including humans. It is worth investigating if chronic lesions require a different treatment protocol than active lesions.

Another important contributor to the number of infectious animals in a herd are animals with recurring active lesions. Previous work reported recrudescence of lesions in up to 54% of treated lesions (Read and Walker, 1998b; Berry et al., 2012; Gomez et al., 2015; Krull et al., 2016b). Gomez et al. (2015) identified that there are three types of animals based on the number of M2 lesions identified during a six month period as pregnant heifer: type I animals had no M2 lesion, type II animals had a single M2 lesion, and type III animals had two or more M2 lesions. It is therefore important to identify those type III animals and to remove them from the herd as they are likely to play an important role in keeping digital dermatitis endemic in a herd.

Reducing Disease Transmission

A general rule to reduce disease transmission is to isolate infectious animals from susceptible animals. With all lesion stages of digital dermatitis considered infectious and in general more than 20% of animals in the herd with lesions, this control measure currently is very impractical. One way to help provide biocontainment of infectious material in herds is the application of bandages on lesions until healed to unaffected skin. Although having to apply and manage bandages in over 20% of the animals in a herd also requires a considerable effort and attention to detail. Biemans et al. (2018) studied the contribution of different disease classes to the transmission of digital dermatitis. They concluded that the basic reproduction ratio for digital dermatitis was almost completely determined by the chronic M4-stage and that reducing the number of M4 lesions in the herd is key to decrease the prevalence of digital dermatitis in a herd. This reiterates that we should not accept chronic digital dermatitis lesions as normal and the need for novel treatment protocols which result in a transition to unaffected skin.

Apart from infectious animals, slurry is considered a major source for disease transmission. *Treponema* spp. have been identified in environmental slurry samples in herds with digital dermatitis, but not in herds which are free from digital dermatitis (Klitgaard et al., 2017). Bell (2017) detected treponemal DNA in floor footprints from cattle, with the majority of positive footprints originating from feet with a digital dermatitis lesion. These findings indicate that decreasing contact with slurry, plays a significant role in decreasing disease transmission within a herd. The results from Chapter 6 support this with mainly housing related risk factors, including cubicle dimension and slurry management, explaining the positive association between total risk score from a risk assessment questionnaire and digital dermatitis prevalence (Vanhoudt et al., 2021). Routine foot disinfection through footbathing is a well-known control measure to reduce transmission of digital dermatitis through contact with slurry. Many studies investigated several aspects of footbathing and were summarized in reviews by Cook (2017) and Jacobs et al. (2019).

Another transmission route considered relevant is through contaminated foot trimming equipment. *Treponema* spp. were first identified and cultured from foot trimming equipment after trimming a cow with digital dermatitis by Sullivan et al. (2014). Gillespie et al. (2020b) confirmed the ability of *Treponema* spp. to survive on foot trimming equipment for up to two hours after inoculation of the foot trimming knives with digital dermatitis *Treponema* spp.. The same research group also detected viable *Treponema* spp. on foot trimming knives when they were used to debride digital dermatitis lesions during trimming (Gillespie et al., 2020b). During the same field study, they also successfully tested a rapid disinfection protocol for foot trimming knives, consisting of a brief rinse of the knifes in water to remove gross contamination followed by a 20 seconds immersion in either of three disinfectants (2% Virkon®, 2% sodium hypochlorite, 1:100 FAM30®; Gillespie et al., 2020b).

For all of the above mentioned transmission routes, current evidence as potential transmission route lies in demonstration of viable *Treponema* spp. and likelihood of direct contact with naive animals (Gillespie and Evans, 2020). Future research should aim to confirm possible transmission routes in experimental studies demonstrating digital dermatitis lesion development in naive animals.

Decreasing the Susceptibility of the Host

Several studies identified the potential for genetic selection to decrease the susceptibility for digital dermatitis in cattle (Biemans et al., 2019b; Oelschlaegel et al., 2022). It would be interesting to investigate how these genotypes relate to the phenotypes based on recurrence of M2 lesions (type I, type II, and type III) as identified by Gomez et al. (2015). Another option to decrease the susceptibility of cattle for digital dermatitis would be by modulating their immune response. However, possibly due to the polymicrobial etiology of digital dermatitis, current efforts to develop an effective vaccine are unsuccessful and future research should look at other options to modulate the immune response to digital dermatitis. Although the genetic background and immune response of cattle in relation to digital dermatitis have a role to play in effective control of digital dermatitis, they are outside the scope of this thesis and will not be discussed further.

BLUEPRINT TO SUBSTANTIALLY REDUCE THE PREVALENCE OF DIGITAL DERMATITIS IN A DAIRY HERD

Complete cure or elimination of digital dermatitis from farms is difficult and was reported only once (Yeruham and Perl, 1998). My recommended approach to substantially reduce the prevalence of digital dermatitis in a dairy herd expands on the 'blitz' approach by Pedersen (2019) and the topical treatment protocol by Alsaaod et al. (2022). It involves the screening of all age and production groups on the farm using pen walks or in-parlor scoring to identify animals with any digital dermatitis lesion. Thereafter, all digital dermatitis lesions receive topical treatment. The treatment protocol consists of (1) thorough cleaning of the lesion and an extensive area of the surrounding skin using water; (2) debridement of necrotic tissue, crusts, hypergranulation tissue, or a combination of these – with the use of local anesthesia if necessary; (3) gentle drying of the lesion using a paper towel; (4) application of salicylic acid paste covering the entire lesion; and (5) application of a bandage consisting of a water-repellent compress, cotton wool, cohesive tape, and kept in place with an adhesive tape (Figure 7.1). In addition, treated animals that are lame would also receive a non-steroidal anti-inflammatory drug. Bandages are kept in place for one week and the topical treatment protocol is repeated until transition to the M0-stage is reached.

To maximize the effect of this collective treatment approach, the timing should be aligned with turning cows out onto pasture. This provides the opportunity to segregate affected animals under treatment, that are kept inside, from animals without lesions, that are out on pasture. Another benefit of timing the collective treatment with turn-out is that the infection pressure for digital dermatitis in general is lower on pasture in comparison with when housed.

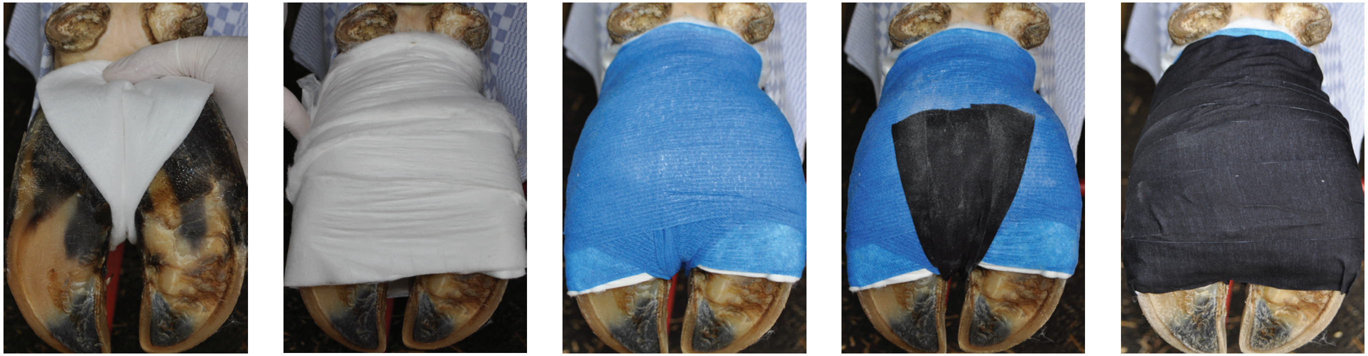

Figure 7.1. Photographs depicting the bandaging technique as described in Alsaaod et al. (2022) with from left to right the application of a water-repellent compress, cotton wool, cohesive tape, and adhesive tape. Photographs courtesy of M. Alsaaod.

In order to maintain a low prevalence of digital dermatitis in the herd, the collective treatment approach should be followed by a control plan which deals with the risk factors for digital dermatitis and has a rigorous footbathing regime to minimize the incidence of digital dermatitis. The control plan should also have a monitoring system in place for early detection of new or repeat cases of digital dermatitis and animals with lesions recurring more than once should eventually be culled.

This is a very intensive protocol and motivation of the farmer is key for it to be successful. While this protocol provides a means to substantially reduce digital dermatitis in a dairy herd, addressing the main cause of lameness in a herd is crucial and this may not always be digital dermatitis. Alongside having technical knowledge, being able to guide the farmers in finding their motivators and solutions that work on their farms is paramount for any disease control plan to be effective. Although preliminary work has been done (Leach et al., 2010a; b; Ivemeyer et al., 2015), there is a need to further our understanding of the intersection between veterinary medicine, communication, and sociology.

CONCLUSIONS

Managing digital dermatitis in dairy herds relies on the early detection and prompt effective treatment of lesions, combined with controlling transmission of the disease within the herd. To date, the detection of digital dermatitis remains time-consuming, especially when done frequently to allow early detection of active lesions. Techniques using computer vision and artificial intelligence seem to have the best potential to automate digital dermatitis detection. The treatment of digital dermatitis currently focuses on topical treatment of active lesions to deal with the negative effect on production and animal welfare. Yet most treatment protocols result in the transition of lesions to the chronic stage and few achieve high levels of cure to unaffected skin, including bacteriological cure. With several non-antibiotic products resulting in similar or better treatment outcomes, there does not seem to be a role for topical antibiotics in the treatment of digital dermatitis. Although the evidence is still weak, the use of bandages appears to result in better cure rates. Controlling digital dermatitis at the herd level includes reducing the number of infected animals through lowering the prevalence of animals with chronic lesions by including them in the treatment strategy, avoiding disease transmission by minimizing the contact of cows' feet with slurry, and decreasing the susceptibility of the herd for digital dermatitis through genetic selection. Bringing all these factors together not only requires farm advisors to be knowledgeable, but they will also need to be good communicators and strong motivators.

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Chapter 8

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Talent wins games,

but teamwork and intelligence

win championships.

Michael Jordan

Chapter 9

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Chapter 10

Biography

Arne Vanhoudt was born on Monday 20th of August 1984 in Hasselt, Belgium. He studied Veterinary Medicine at Ghent University, Belgium, and graduated in 2009. His master thesis was on the transition management of dairy cattle. After graduating, he moved to the UK where he first spent some time in farm animal practice, followed by a residency of the European College of Bovine Health Management at The Royal Veterinary College, University of London, UK. During his time at The Royal Veterinary College, he obtained an MSc in Veterinary Medicine. Beside his teaching and research activities, Arne was also involved in performing animal welfare audits at dairy farms for a British supermarket. In 2015, he moved to the Netherlands and obtained a position at the Faculty of Veterinary Medicine, Utrecht University. In 2016 he became an EBVS® boarded Diplomate of the European College of Bovine Health Management. Arne started working on his PhD in 2017 in combination with teaching. During his time at Utrecht University, Arne obtained the Basic Teaching Qualifiaction of Dutch Universities and the article 9 certificate in Laboratory Animal Science. He co-organized the European Bovine Congress 2019 in ‘s Hertogenbosch, the Netherlands. From 2020 until 2022, Arne was a member of the examination committee of the European College of Bovine Health Management. Since May 2022, Arne works at Royal GD, where he is involved in national disease surveillance of cattle, bovine foot health, and research. Arne is a member of the Dutch hoof trimming association and a RoMS certified cattle mobility scorer.

Chapter 11

Academic Output

PUBLICATIONS

Vanhoudt, A., C. Jacobs, M. Caron, H.W. Barkema, M. Nielen, T. van Werven, and K. Orsel. 2023. Broad-spectrum infrared thermography for detection of M2 digital dermatitis lesions on hind feet of standing dairy cattle. PLoS ONE 18:e0280098. doi:10.1371/journal.pone.0280098.

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ORAL PRESENTATIONS

A cross-sectional study of footbath hygiene and the application of footbathing for control of bovine digital dermatitis on dairy farms. 2023. European Buiatrics Congress 2023, Berlin, Germany.

Bovine digital dermatitis: Trick or treat. 2022. 21st International Symposium & 13th International Conference on Lameness in Ruminants, Minneapolis, USA.

M-score and wound healing assessment of two non-antibiotic topical gel treatments of active digital dermatitis lesions in dairy cattle. 2022. European Veterinary Conference Voorjaarsdagen, Amsterdam, the Netherlands.

Interobserver agreement of digital dermatitis M-scores for photographs of hind feet from standing dairy cattle. 2019. 20th International Symposium & 12th International Conference on Lameness in Ruminants, Tokyo, Japan.

Udder health in the Netherlands after the introduction of the guideline on antibiotic dry cow therapy. 2018. Symposium Droogstand op maat, Wageningen, the Netherlands.

The enforced transition from blanket dry cow therapy to selective dry cow therapy in the Netherlands: An evaluation of the effect on udder health parameters. 2017. European Veterinary Conference Voorjaarsdagen, Amsterdam, the Netherlands.

Monitoring cow comfort and rumen health on a farm with an automated milking system. 2015. National Veterinary Congress of the Dutch Royal Veterinary Orginazation KNMvD, Utrecht, the Netherlands.

POSTERS

An observational study on managing digital dermatitis through risk assessment and veterinary advice on 19 Dutch dairy herds. 2022 World Buiatrics Congress, Madrid, Spain.

Topical treatment of active digital dermatitis lesions with an enzyme alginogel or copper and zinc chelates gel fail to achieve high cure rates to M0 within 10 days. 2022 World Buiatrics Congress, Madrid, Spain.

Farm workers are exposed to substantial levels of formaldehyde on dairy farms. 2022. 21st International Symposium & 13th International Conference on Lameness in Ruminants, Minneapolis, USA.

A risk assessment alone is insufficient to decrease the digital dermatitis prevalence on dairy herds. 2022. 21st International Symposium & 13th International Conference on Lameness in Ruminants, Minneapolis, USA.

Development of an online training tool for the M-score of bovine digital dermatitis lesion. 2022. 21st International Symposium & 13th International Conference on Lameness in Ruminants, Minneapolis, USA.

Automated on-farm detection of M2 lesions with infrared thermography is unlikely. 2022. 21st International Symposium & 13th International Conference on Lameness in Ruminants, Minneapolis, USA.

Can less be more in dry cow therapy? A message from the Netherlands. 2018. Total Dairy Seminar. Stratford-upon-Avon, UK.

Variations in clinically relevant behaviours in a zero-grazed voluntary-milking Holstein herd. 2013. Britisch Catte Veterinary Association Annual Congress. Harrogate, UK.

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