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CLINICAL RESEARCH

Multicenter study investigating long-term survival after synovial lavage of contaminated and septic synovial structures in horses presented to 10 UK referral hospitals

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Abstract

Objective: To report the long-term survival of adult horses that were subjected to synovial lavage for treatment of contaminated and septic synovial structures.

Study design: Multicenter, prospective observational trial.

Animals: Horses ($n = 240$) presented for synovial sepsis at 10 UK referral centers.

Methods: Data for horses presented for treatment of synovial sepsis were collected over a 15 month recruitment period. Owners were contacted a minimum of 365 days after surgery using a structured client interview to assess long term survival. Descriptive statistics, and univariable and Cox proportional hazards models for postoperative survival time were developed.

Results: Survival to discharge was 228/240 (95%) and overall long-term survival was 89.4% (185/207). Unknown cause of injury ($p = .017$), increasing duration of surgery ($p = .003$), increasing weight ($p = .008$), forelimb injuries ($p = .027$), and type of synovial structure ($p = .008$) were found to be associated with death using Cox proportional hazards models.

Conclusion: This study provides information on risk factors associated with survival and death after treatment for synovial sepsis at referral hospitals in the UK. Survival to discharge and long-term survival was excellent. Heavier horses, injuries affecting the forelimbs, tendon sheaths and bursae were

Abbreviations: CI, confidence interval; h, hours; HR, hazard ratio; IV-RLP, intravenous regional limb perfusion; kg, kilogram; L, litres; PMMA, polymethyl-methacrylate; PTS, horses that were euthanized; Ref., reference; spp, species; SPSS, Statistical Package for the Social Sciences; STD, survived to discharge; TP, total protein; UK, United Kingdom; WB, Warmbloods.

associated with poorer long term outcomes. Longer duration of surgery was also found to be associated with a worse prognosis.

Clinical significance: These findings help to provide prognostic information for owners and veterinarians treating horses with synovial sepsis.

1 | INTRODUCTION

Synovial sepsis or contamination is a potentially career-ending and life-threatening condition affecting horses.[1,2] Treatment, in the majority of cases, involves aggressive and thorough lavage and appropriate antimicrobial therapy to eliminate the infection and restore a normal synovial environment.[1–3] The presentation in adult horses differs somewhat from that in foals. In adult horses, the condition most commonly occurs due to a traumatic or penetrating injury to a synovial structure;[2–5] however, in foals, synovial sepsis most commonly occurs due to hematogenous spread, often because of failure of passive transfer and/or secondary to another infection.[6]

Reported survival after synovial sepsis varies between 44 and 90%,[2,3,7–9] showing that, despite appropriate treatment for this condition, there a substantial number of cases still result in mortality. The identification of risk factors that influence this outcome is vital in order to provide veterinarians with evidence-based guidelines to aid case management. In the literature, only a small number of studies use multivariable analysis to investigate factors associated with short-term and long-term survival after treatment and the factors that have been identified differ between studies and lack consistency.[10] There are only a small number of studies that involve multiple centers[7,11] or use a prospective study design.[12]

The evidence to guide clinical decision making is currently limited and further research is needed to provide clarity on what factors are associated with survival to improve outcomes. The objectives of this study were to report the long-term survival of adult horses that were subjected to synovial lavage for treatment of contaminated and septic synovial structures from multiple referral centers within the UK. Another aim of this study was to identify risk factors associated with reduced long-term survival of these horses. We hypothesized that the long-term survival of adult horses with synovial sepsis treated with synovial lavage would be excellent.

2 | MATERIALS AND METHODS

2.1 | Case selection

A prospective, multicenter study was performed to investigate survival after treatment for synovial sepsis. Ten equine referral hospitals in the UK were enrolled in the study based on their caseload, the presence of at least one Diplomate of the European College of Veterinary Surgeons and their willingness to contribute cases. Horses were included if they were presented for treatment of synovial sepsis to one of the enrolled hospitals during the recruitment phase (October 1, 2019 to January 1, 2021) and were subjected to synovial lavage. Horses that were not subjected to any surgical treatment were excluded, as were horses that were euthanized prior to or during the surgery. Synovial lavage was defined as any surgical procedure under standing sedation or general anesthesia, which involved either endoscopic lavage, an open approach, or a through-and-through needle lavage for the treatment of a contaminated or septic synovial structure. Through-and-through needle lavage involved more than two needles within the synovial structure at different locations to facilitate lavage and drainage. An open approach was defined as an arthrotomy (larger incision into a joint) or equivalent larger incision into a tendon sheath or bursae with the incision left open to facilitate postoperative drainage. The inclusion criteria for cases was kept as broad as possible to align the study to represent findings in horses presented for treatment in the UK.[10] Adult horses more than 6 months old were recruited. Cases of synovial sepsis or contamination included two or more of the following:

- Clinical findings: Horse with lameness localized to a synovial structure, synovial effusion, heat or pain on palpation.
- Evidence of direct communication of a wound, a failure of a positive pressure distension test (pressure within the joint or synovial structure not being maintained), or diagnostic imaging findings showing synovial contamination or foreign body penetration into a synovial structure.
- Synoviocentesis parameters indicating an above-normal range: An elevated total nucleated cell count of greater than 10×10^9 cells/L, a total protein concentration greater than 20 g/L and polymorphonuclear cell count percentage greater than 75%. (The normal synovial reference range used was a total nucleated cell count $<1 \times 10^9$ cells/L and total protein concentration <20 g/L.[13,14])
- Horses with a positive bacterial culture from a synoviocentesis sample.

2.2 | Data collection

Data were captured using standardized collection forms that were tested initially in a small pilot study at one hospital prior to commencing the study. To investigate long-term survival, a structured client interview was developed and owners and/or referring vets were contacted following discharge from the hospital. The structured client interview contained questions about ownership, current use of the horse, death including date of death or sale and cause if applicable. The structured client interview was conducted a minimum of 365 days after discharge from the hospital to investigate long-term outcome.[15] All horses remained in the study until they died or were lost to follow up. The structured client interview follow up was conducted by the primary researcher (TDS) at nine hospitals, and by in-house veterinarians at one hospital. Horses were lost to follow up if there was no response after at least three failed attempts to contact. The study design and protocol was reviewed and approved by the University of Nottingham ethics committee. Informed client consent was obtained for participation within the study. If it was not obtained the horse was excluded.

2.3 | Statistical analysis

Variables were assessed and appropriate biological grouping was performed prior to further analysis. Descriptive statistics were calculated for all variables. Survival time was calculated from the date of admission to the date of death or censoring. Cases were censored if they were lost to follow up or if the case was still alive at the end of the study period. If the horse was lost to follow up, the date when the horse's status was last known was used (the date of discharge from the hospital or otherwise). Kaplan–Meier graphs were used to compare variables and explore the probability of survival. Univariable analysis was performed on all explanatory variables to identify any variables associated with survival to discharge. Those variables showing a moderate association ($p < .2$) were then included within multivariable analysis. Correlations between continuous variables were assessed using Pearson correlation coefficients and if they were greater than 0.8 then the most biologically plausible variable was chosen. Correlations between categorical variables were explored using Cramer "V" statistical calculations. Variables with more than 25% missing values were excluded from further analysis. A forwards stepwise elimination procedure was used to create Cox proportional hazards multivariable models. Variables were assessed with a likelihood ratio statistic and remained in the multivariable model if they improved the fit of the model and $p < .05$. Models were created around different points within the clinical presentation and decision making during a case. These time points created the following models; preoperative and intraoperative (model 1); and preoperative, intraoperative and postoperative models (model 2). All variables were then forced back into the model, including those with more than 20% missing data, and model fit was assessed based on likelihood ratio statistics. Cox proportional hazards assumptions were assessed graphically with Schoenfield residuals. Delta-beta values were calculated and any cases contributing to large delta-beta values (<0.4 or >0.4) were excluded and the model was then reanalyzed. Interaction terms of biologically plausible associations were explore. Any associations where $p < .05$ were included within the model and the model analyzed.

Statistical analysis was performed using SPSS (Version 28, IBM). Statistical significance was set at $p < .05$.

3 | RESULTS

The horses ($n = 240$) underwent surgical treatment at the referral hospitals during the recruitment period and recovered from the surgical procedure. No horses were euthanized on the surgical table. Lavage was performed on 234 horses under general anesthesia, and six horses had lavage performed under standing sedation. Of the 240 horses, 104 were female (43.3%) and 136 were male (56.7%). The median age was 8 years old (range 1–26 years). There were 96 Thoroughbreds or Thoroughbred crosses, 20 Cobs, 86 Warmbloods (WB) or WB crosses, 18 ponies or Arabs, 14 Draft breeds and six other breeds. Median weight was 513.5 (range 175–786 kg). One synovial structure was affected in 216 horses, 21 had two structures affected, and three horses had three structures affected. The most common synovial structure involved was the metacarpophalangeal or metatarsophalangeal joint (59 horses, 24.6%), followed by the digital flexor tendon sheath (42 horses, 17.5%) and the tarsocrural joint (29 horses, 12.1%). The forelimb was involved in 105 horses (43.8%) and the hindlimb was involved in 135 horses (56.3%). The cause of injury was from a kick or trauma in 103 horses (42.9%), a thorn penetration in 37 horses (15.4%), a wire or other foreign body in 27 horses (11.3%), it was unknown in 53 horses (22.1%), and other causes were involved in 20 horses (8.3%), which included 10 horses due to iatrogenic causes. For these 10 horses, the injuries in two were due to intrasynovial medication with corticosteroids and two occurred after routine elective orthopedic surgery. Insufficient data was recorded for the other six cases. Table 1 outlines the interval between the injury occurring prior to admission at the hospital. This shows that most horses

TABLE 1 Interval between the injury occurring and admission at the hospital.

Duration of injury prior to admission	Number of horses
Within 12 h of injury	66
12–24 h after injury	85
1–7 days after injury	32
More than 7 days	35
Unknown	22

(151/240) presented within 24 h after injury in this study. Most horses were administered antimicrobials prior to admission at the hospital (126/240, 52%) with 80/240 (33%) of horses being administered a combination of intramuscular procaine penicillin and intravenous gentamicin. Only 34/240 had intrasynovial antimicrobials administered before admission to the hospital. Nonsteroidal anti-inflammatories were administered to 134 horses (56%) prior to referral with the majority given intravenous flunixin.

Synoviocentesis on admission was performed in 190 horses (190/240, 79.2%) and not performed in 35 horses (14.6%). The median white-cell count on admission was 63 $\times 10^9$ cells/L (range 1–352 $\times 10^9$ cells/L), median total protein concentration of 42 g/L (range 2–94 g/L) and a median polymorphonuclear cell count 83% (range 23%–100%). There were 96 horses that had a synovial fluid sample submitted for bacteriology, and of these 64/96 (66.6%) had a positive culture. The details of culture technique were not recorded. Table 2 presents the bacterial species cultured (Table 2).

Of the horses presented, 170 had wounds (170/240, 70.1%). The median size of the wounds was 3 cm (range 1–20 cm). When the depth of wound was reported, 13 were partial or superficial skin thickness, 102 were full skin thickness and 40 wounds had deeper tissues exposed. The surgical technique was performed under general anesthesia in 234/240 horses (97.5%), and under standing sedation in 6/240 horses (2.5%). A median volume of 10 L was used for lavage of the primary synovial structure (range 2–30 L). The median surgery time was 60 min (range 25–180 min) and median general anesthesia time was 90 min (range 30–200 min).

Table 3 presents the main surgical findings identified. Of the 170 horses that had wounds, 138 were debrided (138/170, 81.1%), with 124 using sharp resection (with blade or other surgical instrument) (124/138, 90%), 14 horses had a combination of hydrosurgery and sharp resection (14/138, 10%). Details of wound closure were available for 136 horses (136/170, 80%), with 19 left partially or completely open to facilitate drainage. Four horses had active drains used and seven horses had Penrose drains inserted. The type of synovial lavage was described in all horses with most horses having endoscopic lavage (222/240, 92.5%) and a small number having through-and-through needle lavage (18/240, 7.5%). The size of needles or number of needles used was not specified in any case. The median volume of lavage fluids used for horses undergoing through-and-through lavage under standing sedation was 4 L. The median volume of lavage fluids used for horses undergoing through-and-through lavage under general anesthesia was 5 L. The median volume of fluids used for horses undergoing endoscopic lavage under general anesthesia was 10 L.

Most horses had one synovial lavage (209/240, 87%) with 26/240 (11%) having two synovial lavages and 5/240 (2%) having three synovial lavages. Of the horses having three synovial lavages, 4/5 (80%) had endoscopy and 1/5

TABLE 2 Distribution of bacteria cultured from synovial structures obtained from preoperative and intraoperative sampling.

Family	Species	Number of cases
Streptococcaceae	*Streptococcus equi subsp. Zooepidemicus*	18
	Other *Streptococcus* spp.	3
	Beta-hemolytic *Streptococcus* spp.	3
	Streptococcus dysgalactiae subsp. Equisimilis	1
Bacillaceae	*Bacillus cerus*	7
Enterococcaceae	*Enterococcus faecalis*	1
	Other *Enterococcus* spp.	1
Enterobacteriacae	*Escherichia coli*	8
	Proteus spp.	2
	Enterobacter spp.	2
Psuedomondaceae	*Pseudomonas aeruginosa*	4
Staphylococcaceae	Coagulase negative *Staphylococcus* spp.	5
	Not specified	5
	Staphylococcus hemolyticus	1
	Staphylococcus aureus	8
Other bacteria	*Pasteurella* spp.	2
	Actinobacillus	5
Not specified		9
Number of bacteria		
1 bacteria		46
2 bacteria		15
>2 bacteria		3

TABLE 3 Main surgical findings of 240 horses presented for synovial sepsis.

Surgical finding	Number of horses
Surgical technique	
Endoscopy	222
Other	18
Presence of osseous pathology	
Present	43
Not present	180
Not recorded	17
Presence of cartilage pathology	
Present	39
Not present	151
Not recorded	50
Presence of soft tissue pathology	
Present	51
Not present	133
Not recorded	56
Presence of pannus	
Mild	63
Moderate	30
Severe	33
Not recorded	106
Synovial inflammation	
Mild	69
Moderate	45
Severe	23
Not recorded	85
Presence of foreign material	
Present	49
Not present	156
Not recorded	35

Note: The description of the degree of pannus as mild, moderate or severe was left to the surgeon's discretion as there are no current recommended guidelines on severity scales. Synovial inflammation was graded depending on the presence of the following characteristics: hyperemia, petechiation, and proliferation and stunting of the synovial villi. These characteristics were grouped so that the presence of one characteristic related to mild inflammation, two or three related to moderate inflammation, and if all four were present then this equated to severe synovial inflammation.

(20%) had through-and-through lavage. Of the horses that had two synovial lavages, 3/26 (11.5%) had through-and-through lavage and 23/26 (88%) had endoscopic lavage. Of the horses having one synovial lavage, 14/209 (7%) had through-and-through lavage and 195/209 (93%) had endoscopic lavage. This resulted in 4/18 (22%) of horses with through-and-through lavage and 27/222 (12%) of endoscopic procedures requiring repeat synovial lavage.

Intrathecal antimicrobials were used in 223 horses, with the most common antimicrobial used being amikacin ($n = 207$) and gentamicin ($n = 11$) when specified. Antimicrobial implants were used in 16 horses, with three horses having an intrasynovial catheter placed and these were all used for treatment of septic calcaneal bursas. Two horses had polymethyl-methacrylate (PMMA) beads used intra-articularly, and 11 horses had collagen sponges used in an extrasynovial location within wounds. Two horses had both intrasynovial and extrasynovial antimicrobial implants used. Three horses had intraoperative intravenous regional limb perfusion performed (IV-RLP). All horses recovered from general anesthesia without complication.

Postoperatively, 130 horses had intrasynovial medication performed (130/240, 54%), and the most common antimicrobial was amikacin (118 horses), then gentamicin (nine horses). The dose of intrathecal amikacin used was 100 mg in 26 horses, 200 mg in 17 horses, 300 mg in 11 horses, 400 mg in two horses, and 500 mg in 55 horses. Intrathecal medication was performed once in 29 horses, twice in nine horses, three times or greater in three horses. Intravenous regional limb perfusion was performed in 66 horses postoperatively (66/240, 28%), most commonly using gentamicin (56 horses), amikacin (6 horses), and ceftiofur (2 horses). It was performed once in 32 horses, twice in 25 horses, and three times or greater in eight horses. Horses were treated for a median of 10 days of antimicrobial treatment with a range of 1–36 days recorded. Most horses were treated with a combination of procaine penicillin and gentamicin (200 horses). Most horses had synoviocentesis performed postoperatively 138/240 (57.5%). Twenty-two horses (22/138, 16%) had three or more synoviocentesis samples taken, 60/138 (43%) horses had two synoviocentesis samples taken and 56/138 (41%) horses had one synoviocentesis sample taken.

Of the 240 horses that recovered from the first surgical procedure, 228 horses (95%) survived to discharge from the hospital. All 12 horses that did not survive to discharge from the hospital were euthanized due to unresolved synovial sepsis. The median number of days of hospitalization was 7 days (range 1 and 36 days). Figure 1 shows the number of surgical procedures and the response of horses to treatment. Table 4 shows the details of the discharge medications of the 228 horses leaving the hospital. One hundred and sixty two horses were discharged with antimicrobials (159/228, 69.7%). The median duration of discharge antimicrobials was 5 days (range 2–19 days). The three main oral drugs for horses to be discharged with were trimethoprim sulfonamides (97/159, 61%), enrofloxacin (28/159, 17.6%), and doxycycline (27/159, 16.9%). For those horses discharged on enrofloxacin, in 16 cases this was reported to be based

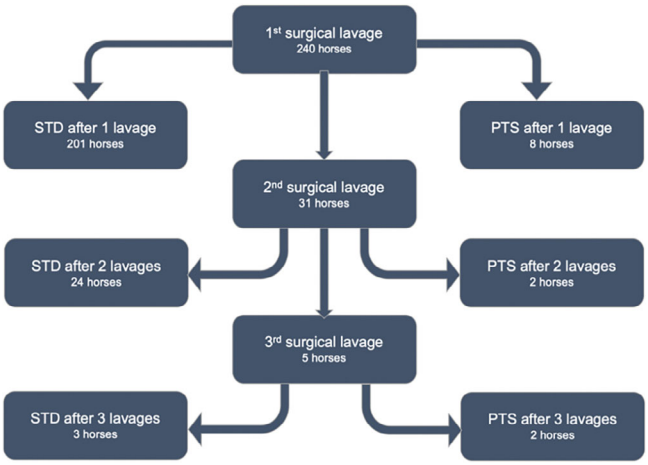

FIGURE 1 Flow chart showing the movement of horses and their response to surgical treatment until discharge from the hospital. PTS, horses that were euthanized; STD, survived to discharge.

TABLE 4 Medications of horses that were discharged with after treatment for synovial sepsis.

Discharge data	Number of horses
Discharged with antimicrobials	
Yes	162
No	64
Unknown	14
Trimethoprim sulfonamides	97
Doxycycline	27
Enrofloxacin	28
Other	7
Discharged with analgesia	
Yes	124
No	63
Unknown	53
Phenylbutazone	119
Other	5

on culture and sensitivity results taken from synovial samples, in two cases this was not based on culture and sensitivity results, and this was not recorded in 10 cases. For those horses discharged with trimethoprim sulfonamides and doxycycline, these were based on culture and sensitivity results in 20/97 (21%) and 8/27 (30%) cases respectively.

When investigating long-term survival, 33 horses were lost to follow up after hospital discharge (33/240,14%), leaving 207 horses available for analysis (207/240, 86%). The long-term survival of the horses in this study was 89.4% (185/207) at 365 days after surgery and 10.6% (22/207) were dead. Of the horses that died, 20 horses died due to reasons associated with synovial sepsis and two died for reasons other than synovial sepsis (fracture = 1, colic = 1). The median duration of follow up was 517.5 days (range 2 days – 917 days).

The results of the univariable analysis of continuous and categorical variables associated with survival time are presented in Supporting Information, S1 and S2. The results of the Cox proportional hazards models for factors associated with death following treatment for synovial sepsis are presented in Table 5. No associations were identified when preoperative variables were considered on their own. When preoperative and intraoperative variables (model 1) as well as preoperative, intraoperative and postoperative variables (model 2) were assessed, this identified that cause of injury (known/unknown) and increasing duration of surgery were associated (p <.05) with increased likelihood of death. When the type of synovial structure affected was forced back into the model (model 3) this identified that the limb affected (forelimb or hindlimb) (hazard ratio (HR) 0.085, 95% confidence interval (CI) 0.010–0.754, $p = .027$), increasing weight (HR 1.011, 95% CI 1.003–1.019, $p = .008$), cause of injury (known/unknown) (HR 9.391, 95% CI 1.790–49.264, $p = .008$), increasing duration of surgery in minutes (HR 1.059, 95% CI 1.024–1.096, $p = <.001$), and the type of synovial structure (joint, tendon sheath or bursa) (HR 7.685, 95% CI 1.075–54.917, $p = .042$) affected showed an association with death. To demonstrate the results of these models, if a horse had a surgery duration of 90 min, compared with 60 min, they had a 2.35 times greater risk of death. A horse with a weight of 500 kg compared to a horse with a weight of 400 kg is 2.97 times more likely to die.

4 | DISCUSSION

This study provides information on risk factors associated with survival and death after treatment for synovial sepsis at referral hospitals in the UK. Long-term survival to 1 year after surgery was 89.4% and factors identified as associated with death were unknown cause of injury, increasing duration of surgery, increasing weight, limb affected (forelimbs), and type of synovial structure (bursa and tendon sheaths).

In this study, it was chosen to investigate risk factors affecting long-term survival rather than survival to discharge, which has been used previously.[3,4,7] Long-term survival takes into account those horses that may be euthanized shortly after discharge from the hospital, and is felt to be a more accurate representation of the survival rate. Long-term survival is used and recommended in

TABLE 5 Multivariable Cox proportional hazards models with risk factors associated with death in 240 horses presented for treatment of synovial sepsis at 10 referral hospitals.

Variable		B	SE	Significance	Hazard ratio	95.0% CI for Exp(B)	
						Lower	Upper
Model 1: Preoperative and intraoperative variables							
Cause	Known	Ref.					
	Unknown	1.665	0.725	0.022	5.288	1.277	21.905
Duration of Surgery	Minutes	0.029	0.010	0.003	1.029	1.010	1.049
Model 2: Pre, intra and postoperative variables							
Duration of surgery	Minutes	0.029	0.010	0.003	1.029	1.010	1.049
Cause	Known	Ref.					
	Unknown	1.758	0.735	0.017	5.802	1.375	24.483
Model 3: Synovial structure and model 2							
Limb affected	Forelimb	Ref.					
	Hindlimb	−2.466	1.114	0.027	0.085	0.010	0.754
Weight	kg	0.011	0.004	0.008	1.011	1.003	1.019
Cause	Known	Ref.					
	Unknown	2.240	0.846	0.008	9.391	1.790	49.264
Duration of Surgery	Minutes	0.058	0.017	<0.001	1.059	1.024	1.096
Type of synovial structure affected	Joint	Ref.		0.008			
	Tendon sheath	2.039	1.003	0.042	7.685	1.075	54.917
	Bursa	3.918	1.287	0.002	50.283	4.039	625.963

Abbreviations: B, estimated coefficient; CI, confidence interval; Exp(B), exponential value of the estimated coefficient; kg, kilogram; Ref., reference; SE, standard error; TP, total protein.

human follow-up studies as it represents the "true" survival rate and will account for any late adverse effects after discharge from the hospital. Premature termination of follow up can lead to a distorted view of a treatments value.[16] Interestingly, the survival rate of 89.4% was similar to other recent studies reporting survival to discharge (86%–90%)[3,4] suggesting that if horses survive to discharge then they are likely to survive in the long term.

A similar rate of success (approximately 90%) is reported for human patients after treatment for septic arthritis.[17,18] A recent study investigating risk factors for death in people identified that older patients, high serum CRP concentrations, patients with other debilitating diseases (diabetes mellitus, bacteremia), and skin involvement with septic arthritis were more likely to die.[17] These factors differ from those previously identified in horses and may be due to different causes of septic arthritis. Comorbidities were not investigated in this study; however, presence of a wound (skin involvement) or increasing age were not associated with an increased risk of death. Interestingly, previous equine studies have found that horses with wounds and synovial sepsis were more likely to survive.[3] This may be due to the different causes of synovial sepsis in people in comparison with horses and the likely earlier recognition of synovial sepsis by horse owners when a wound is visible or the release of inflammatory mediators.[3]

Factors relating to the cause of injury have been identified as affecting the outcome substantially;[3,7,10] however, in this study, if the cause of injury was unknown to the owner or carer, this was associated with an increased likelihood of death, which specifically has not been found previously. Other factors relating to injury type were investigated and it was found that there was no substantial correlation between the time to admission, or the presence of a wound, or the cause of the injury. The importance of the cause of the injury being unknown to the owner is not understood and further investigation is needed. In this study, detailed analysis and comparisons of the known causes of injury was not possible due to the small sample sizes. Within the equine literature, epidemiological studies specifically investigating causes of contaminated synovial structures and synovial sepsis are limited to studies on iatrogenic injury[19–23] and idiopathic causes.[24] There has been some research into risk factors for traumatic injuries occurring in horses

previously[22] and, similarly, in 19% of cases the cause of injury was unknown. Owen et al. found that only a small number of traumatic injuries caused synovial sepsis (1.3%). Further research on specific risk factors for injuries causing synovial sepsis could improve understanding and even help identify management and other predisposing factors and reduce the frequency of synovial sepsis occurring.

The duration of time between injury and admission or treatment has been previously identified by two studies to be associated with poorer outcomes;[5,7] however, in the present study this was found to have no association with long-term survival consistent with other research.[3,9,11] The reason for these differences is unknown but may be because there are multiple factors that could affect the duration of time between the injury occurring and treatment being initiated. Examples of these contributing factors include the early identification of an injury, the availability of transport to a hospital, financial considerations, and initiation of medication prior to admission. Due to the relatively small numbers of cases within these groups, these cannot be fully explored within this study. Interestingly, within the human literature, there appears to be a limited negative effect of a time delay between diagnosis of synovial sepsis and treatment on mortality or morbidity.[25,26] Future equine research is needed, including meta-analysis between studies, before firm conclusions can be made on how duration between injury and treatment affects outcomes following synovial sepsis.

There was no association between surgeries performed out of hours in comparison with surgeries performed within working hours as previously found.[3] This difference may be because the research in the present study was conducted at multiple hospitals rather than at a single center, which could mean that specific hospital factors, such as staffing and resources, are less influential on this variable.[3]

Horses with injuries affecting hindlimbs were less likely to die than horse with forelimbs affected. This has previously been identified as a risk factor[27] and this only became important when synovial structure was considered in the model. Previous authors have hypothesized that this is due to an increased proportion of the horse's weight being distributed through the forelimbs compared to the hindlimbs, so that, if postoperative complications or lameness occurs, it has a greater detrimental effect on the animal.[27,28] Furthermore, in support of this view, heavier horses had an increased likelihood of death in this study. Different horse factors have previously been identified as affecting the outcome, but weight has not been reported.[10]

The type of synovial structure affected was categorized into broad groups including tendon sheaths, bursae, and joints due to the small numbers of cases within each specific synovial structure preventing more detailed analysis. It was found that injuries involving tendon sheaths and bursae were associated with death in comparison with joints. Although this result has not been identified previously, the type of synovial structure has been shown to influence outcomes with earlier studies either incorporating it into multivariable analysis or specifically investigating different synovial structures.[4,5,11] In addition, it has been noted previously that horses with multiple synovial structures[2] or adjacent synovial structures[5] have a worse outcome. The number of synovial structures affected did not affect survival rate. Studies investigating specific synovial structures with larger sample sizes or comparing outcomes could be useful in clarifying this variable further.

Moderate or severe bone or soft tissue involvement, has previously been identified to be associated with death in relation to certain synovial structures such as calcaneal bursae or navicular bursae.[7,11] No substantial association with long-term survival was identified in this study and this may be due to the relatively small numbers of horses identified in these groups. Further investigation into the long-term return to athletic function could further clarify this. Horses that had more than one surgical procedure were found to be associated with increased likelihood of death during univariable analysis, and Milner et al. found increasing numbers of surgical procedures to be associated with death. However, this did not remain in the final multivariable model within this study.

Longer surgery times were associated with an increased likelihood of death. Surgery duration has been found to negatively affect outcome across several different procedures and species due to increased wound exposure, increased risk of surgical site infections, or anesthesia related complications and others; however, it has not previously been identified as important in terms of outcomes after synovial sepsis.[29] Numerous factors could influence surgery duration including different hospital factors, surgeon experience, the synovial structure involved, the complexity of the procedure and the degree of injury.[1] When these variables were assessed during the univariable analysis, no association with death was identified in this study and further investigation into surgery duration and any associated variables is warranted in the future.

Interestingly, approximately 70% of horses were discharged from hospitals with antimicrobials and the median duration of antimicrobial treatment was 5 days. There is discrepancy within the literature on the recommended duration of antimicrobial treatment for synovial sepsis, and there are no proven, rapidly available synoviocentesis parameters to currently help guide this decision

making.[30] In this study, there appeared to be trends with some hospitals routinely discharging horses with antimicrobials and others not doing so. There was no univariable association between long-term survival with horses discharged with antimicrobial medications and those without. In human cases of septic arthritis, shorter durations of antimicrobials have been found to result in similar positive outcomes to longer courses.[31] Further equine studies are required to help guide clinicians to an appropriate length of antimicrobial treatment for individual cases to help prevent antimicrobial resistance. Enrofloxacin was prescribed for discharge in 17.6% of cases and was reported to be based on culture and sensitivity results in 57% of those cases. Ideally, culture and sensitivity results from synovial samples should guide the use of protected antimicrobials, and in those cases where this did not occur, further information was not available to explain the choice of antimicrobial, which is a limitation of this study.

As with many studies, low case numbers and missing data were issues that were encountered. The use of multiple centers from around the UK did improve case numbers; however, case recruitment occurred during the COVID-19 pandemic and this could have influenced the number and distribution of cases presented, owner decisions, and the hospital's management of cases. Selection bias could have also influenced the results presented in this study. Horses that were presented to referral hospitals but not subjected to treatment were not recorded or included. The decision to euthanize a horse is based on numerous factors including financial and emotional concerns. It was therefore elected to exclude these horses and just investigate those that had the opportunity for treatment. However, this could have led to horses that had a poorer prognosis not being subjected to treatment. Contact with the owner was attempted three times, and if there was no response, the case was censored, with 14% of horses lost to follow up within this study, which is less than 20% which is generally classed as acceptable.[25]

The long-term survival rate following treatment of contaminated and septic synovial structures reported in this study was excellent (89.4%), and is similar to that reported in previous studies.[2,3,5,7,9,11,12] Several risk factors associated with a poor outcome have been identified such as increasing surgery duration, increasing weight, and injuries affecting forelimbs, bursae and tendon sheaths. Careful identification of cases preoperatively taking into account these factors will help client communication and manage expectations. Methods to help reduce surgery time and make it as efficient as possible could also improve outcomes in the future. It is hoped the results from this study will provide more evidence to aid case management for clinicians and owners and improve welfare of horses suffering from synovial sepsis.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest related to this report.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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