TITLE: Use of positive contrast radiography to identify synovial involvement in horses with traumatic limb wounds

AUTHORS: Bryant, H A; Dixon, J; Weller, R; Bolt, D M

JOURNAL: Equine Veterinary Journal

PUBLISHER: Wiley

PUBLICATION DATE: 21 June 2018 (online)

DOI: http://dx.doi.org/10.1111/evj.12985

MR. JONATHON DIXON (Orcid ID : 0000-0001-8018-306X)

MR. DAVID M. BOLT (Orcid ID : 0000-0002-0900-5022)

Article type : Article

Use of positive contrast radiography to identify synovial involvement in horses with traumatic limb wounds

H. A. Bryant[1], J. J. Dixon[2], R. Weller[1] and D. M. Bolt*[1]

[1]Royal Veterinary College, Veterinary Clinical Sciences, North Mymms, Hatfield, Hertfordshire, AL9 7TA, UK and [2]Rainbow Equine Hospital, Malton, North Yorkshire, YO17 6SG, UK.

*Corresponding author email: dbolt@rvc.ac.uk

Keywords: horse; septic arthritis; infection; lameness diagnosis; contrast arthrography

Summary

Background: The diagnostic value of positive contrast radiography in the work-up of suspected synovial infection in horses with limb wounds near synovial structures has yet to be systematically evaluated.

Objectives: To determine the specificity, sensitivity and positive and negative predictive values of positive contrast radiography for identification of synovial infection in a population of horses with limb wounds.

Study design: Retrospective case study comparing the performance of positive contrast radiography to the gold standard of synovial fluid cytology in horses presenting with limb wounds in the vicinity of synovial structures.

Methods: Case records of horses presenting to the Royal Veterinary College Equine Hospital between 2010 and 2015 with limb wounds that may have compromised adjacent synovial structures were analysed. Synovial fluid cytology results were used to categorise synovial structures in infected and non-infected groups. Positive contrast radiography results were compared between infected and non-infected groups and sensitivity, specificity, positive and negative predictive values were calculated.

Results: Fifty horses with 66 synovial structures were included in the study. Positive contrast radiography had a high specificity (86.4%), but only a moderate sensitivity (59.1) for the identification of synovial infection. Additionally, a low positive predictive value (68.4%) and high negative predictive value (80.9%) were observed in this population of horses.

Main limitations: Sensitivity, specificity and predictive values may differ between different synovial structures and cases. Different conclusions may be drawn from the results in a single population. Sensitivity and specificity of positive contrast radiography may also be influenced by different techniques used by examiners and by inherent characteristics of individual cases.

Conclusions: Positive contrast radiography should be used for the investigation of potential synovial infection in horses with limb wounds, particularly if no synovial fluid sample for laboratory analysis can be obtained. However, it appears that positive contrast radiography is best used in combination with other tests to ensure that a correct and timely diagnosis is made.

Introduction

Bacterial infections of joints, tendon sheaths or bursae are considered to be life-threatening or career-ending conditions in the horse. Common aetiologies for synovial infection include traumatic injuries, iatrogenic infection following intra-articular injection or (rarely) post-operative synovial infections [1]. Colonisation of a synovial compartment results in an inflammatory response with subsequent release of proteolytic and degradative enzymes, which can cause severe and irreversible damage to the articular cartilage and the soft tissues of the joint. Additionally, within a synovial bursa or sheath, infection has been shown to lead to adhesion formation and fibrosis, both of which can result in chronic lameness [2]. Acute synovitis and capsulitis can be painful and the release of pro-inflammatory mediators, such as metalloproteinases, aggrecanases, prostaglandins, interleukin 1 and TNF-alpha, can contribute to the development of degenerative joint disease and osteoarthritis in the horse [3].

A prompt and accurate identification of synovial infection must occur in order to minimise these detrimental effects that are progressive in nature, and to allow for timely initiation of an effective treatment [4]. Treatment of synovial infection consists of lavage and debridement of the affected synovial structure in combination with systemic and local delivery of antibiotics that reaches or exceeds the effective minimum inhibitory concentration for the bacteria causing the infection [5]. The intended treatment outcome of a complete return to performance in equine patients highlights the importance to correctly and timely diagnose and treat synovial infections [6]. Correct identification of synovial infection can rely on a combination of factors, including history and physical examination, imaging modalities, such as radiography and ultrasonography, and synovial fluid analysis (SFA), with cytological and bacterial analysis and total protein (TP) content of the latter being considered to be of primary importance [1]. Although radiography is not necessarily the primary method used to identify synovial infection, it is used to provide valuable additional information that may confirm contamination of a synovial compartment [7]. Positive contrast radiography can demonstrate the loss of integrity of a synovial capsule, which is particularly valuable in the examination of traumatic wounds within their vicinity [8].

Positive contrast radiography involves the injection of positive contrast material via injection into a synovial compartment from an aseptically prepared site remote to the area of suspected pathology (e.g. solar penetration or wound), followed by radiographic examination (Fig 1). Introducing the needle away from the site of traumatic penetration also reduces the risk of iatrogenic contamination and subsequent infection [9]. A synovial fluid sample for laboratory analysis should be obtained, whenever possible. If no synovial fluid is obtained directly, an injection of sterile physiologic fluid can be performed and a sample re-aspirated for analysis, whilst taking into account the occurring dilution [10]. Subsequently, a radiographic contrast agent, for example iohexol, is injected in undiluted or diluted form, using a volume that will maximally distend the synovial compartment and ensure egress from the potential penetration. Because penetrations occur frequently in the flexed limb and alignment of the defects in skin, subcutaneous tissues and synovial capsule is required to obtain fluid egress, the horse should be walked around the examination room or the limb repeatedly flexed prior to then performing a minimum of two orthogonal radiographic views [9].

The aim of the present study was to evaluate the diagnostic value of positive contrast radiography in the examination of horses with suspected synovial infection due to traumatic wounds in the vicinity of synovial structures. We hypothesised that positive contrast radiography has a high sensitivity and specificity, as well as high positive and negative predictive values, when used for the identification of synovial infection in equine patients with traumatic limb wounds.

Materials and methods

Case records from the Royal Veterinary College Equine Hospital between December 2010 and July 2015 were reviewed to identify horses that presented with a traumatic wound located in the vicinity of a synovial cavity. Horses were included in the study, if both SFA and positive contrast radiography had been performed during the initial work-up and if there was a recorded value for synovial fluid total nucleated cell count and/or total protein.

For each case, clinical parameters were collected. Every synovial structure evaluated was categorised as infected or non-infected, based on the SFA result (“gold standard”). Synovial structures with fluid samples that revealed a total nucleated cell count greater than 30 x 10^9/L and/or a total protein concentration greater than 40 g/L were categorised as infected. Structures with synovial fluid parameters below these thresholds were categorised as non-infected. Results of positive contrast radiography were considered positive and indicative of synovial infection, if the radiographic views demonstrated communication between the examined synovial structure and the adjacent wound. Results of positive contrast radiography were considered negative, if the radiographic views showed an intact synovial capsule with no evidence of contrast extravasation to the surrounding tissues. The retrospective assessment of the positive contrast radiography studies was performed by a single investigator (H.A.B.).

Data analysis

Total protein, total nucleated cell count and differential neutrophil percentages were analysed to determine, if there was a significant difference for each of these parameters between infected and non-infected synovial fluid samples. Distribution of data was evaluated using the Shapiro-Wilk test. If data were normally distributed, Student's t-test was used to compare between infected and non-infected structures. If data were not normally distributed, the Mann-Whitney U Test was used. Categorical parameters between cases in the infected and non-infected groups were compared using Chi squared test and Fisher's Exact test. Significance was set at $p<0.05$.

The correlation between positive contrast radiography and SFA was assessed for each case. The aim was to determine, in how many cases the results of positive contrast radiography came to the same conclusion as SFA with regards to whether or not synovial infection was present. Specificity, sensitivity, as well as positive and negative predictive values were calculated to evaluate the performance of positive contrast radiography [11]. Statistical software (SPSS®Statistics for Windows Version 22[a]) was used for data analysis.

Results

Fifty horses with 66 full-thickness wounds located near synovial compartments were included in the study. Of the 66 synovial structures Included, 22 met the criteria of being infected, whereas 44 were categorised as non-infected.

Of the 22 synovial compartments that were infected, 18 (82%) horses were lame on the affected limb and in 15 (68%) of the examined synovial structures distension was present. Ninety-one percent of infected synovial compartments (n = 20) were surgically treated. The values for synovial fluid total protein, total nucleated cell count and neutrophil count were not normally distributed. Eighty-two percent (n = 18) of infected synovial compartments had reported values for a differential synovial fluid cell count with a median neutrophil percentage of 82.6% (range of 50-98). The synovial fluid total protein was reported in 20 (91%) of cases with synovial infection with a median of 46.5 g/L (range 20-76). The total nucleated cell count was also reported in 20 (91%) cases with synovial infection with a median of 49.15 x 10^9/L (range 10-143). A large variety of synovial structures was affected (Supplementary Item 1) with the most commonly infected structure being the distal interphalangeal joint (n = 4).

Of the 44 synovial compartments that were non-infected, 28 horses (64%) were lame on the affected limb and 20 (45%) had local synovial distension. Sixty-five percent (n = 26) had reported values for a differential synovial fluid cell count with the median neutrophil percentage being 77.6% (range 5-100). The median total protein was in non-infected synovial structures was 19.35 g/L (range 3.5-38.5) and the median total nucleated cell count was 1.7 x 10^9/L (range 0.1-29.4). The most common non-infected synovial compartment investigated was the digital flexor tendon sheath (n = 15), followed by the middle carpal joint (n = 7) and the metatarsophalangeal joint (n = 5). The infected and non-infected synovial compartments are listed in Supplementary Item 1. There was a significant difference between infected and not-infected synovial cavities for total protein (p<0.01), total nucleated cell count (p<0.0001) and neutrophil count (p<0.01), but not for neutrophil percentage (p = 0.13). There was no significant difference between groups for lameness (p = 0.3) and effusion (p = 0.16)

Performance of positive contrast radiography

Positive contrast radiography demonstrated a communication between the traumatic wound and the adjacent synovial compartment in 13 out of the 22 cases where the adjacent synovial compartment was infected. This equates to an agreement of positive contrast radiography and SFA in 59% cases of synovial infection. On the other hand, positive contrast radiography correctly demonstrated the absence of a communication between the traumatic wound and the adjacent synovial compartment 38 out of the 44 non-infected structures (86.4%). Overall, positive contrast radiography correctly identified the infection status of the investigated synovial structure correctly in 51 of the 66 (77.3%) examined synovial compartments. The overall specificity of positive contrast radiography to identify synovial infection was 86.4%, whereas the sensitivity was 59.1% and the positive and negative predictive values were 68.4% and 80.9%, respectively. A list of the synovial structures examined and the results of the positive contrast radiography examination can be found in Supplementary Item 1.

Discussion

Synovial fluid analysis remains the diagnostic gold standard in horses with wounds that are associated with potential synovial infection [1]. The aim of the present study was to evaluate, if positive contrast radiography can be diagnostic or supportive, when used in conjunction with or as an alternative to SFA. Developing and using practical alternative examination techniques is important, as, in many clinical cases, it is not possible to obtain a synovial fluid sample for laboratory analysis [9] or subcutaneous gas accumulation and other wound-related factors prevent effective ultrasonographic examination. Sensitivity of a test is defined as the proportion of subjects with condition that will have a positive result [11]. In this study, the sensitivity of positive contrast radiography to identify synovial infection was 59.1%. This is not particularly high and suggests that positive contrast radiography may be insufficient as a stand-alone test to identify synovial infection. Our findings are in agreement with the statement of Barker (2016) that false negative positive contrast radiography results are not uncommon when examining potential synovial penetrations. The author further indicated that this could be particularly the case in the investigation of possible navicular bursa infection after solar penetrations [9]. Although this is supported by the findings in our study where we were unable to identify established navicular bursa infection with positive contrast radiography in 2 cases, it appears difficult to attribute parameters such as sensitivity, specificity and positive and negative predictive values to the positive contrast radiography examination of synovial structures in different anatomical regions. This can be explained in the low numbers of certain synovial structures examined in our study, but also by the inherent variability in the characteristics of traumatic wounds. It could be speculated that the diameter of a focal penetration injury in the frog is substantially reduced by the elastic properties of the soft horn following removal of a penetrating foreign body. This in return could result in a high resistance of the injected contrast material to be extravasated through the wound canal following distension of the navicular bursa and in a false-negative positive contrast radiography result.

Tests with a high sensitivity are useful for ruling out a condition and a very sensitive test is most valuable, if an individual case tests negative. Due to the fact that the test does not result in many false negatives, it is very likely that an individual with a negative test does not have the condition [12]. Specificity is defined as the proportion of subjects without a condition that will have a negative test result [11]. Tests with a high specificity are therefore useful for confirming the presence of a condition and a very specific test is most valuable in situations where an individual case tests positive [12]. The specificity of positive contrast radiography in our study was high at 86.4%. This could potentially minimise the number of horses undergoing unnecessary endoscopic lavage or other surgical treatment of non-infected synovial structures.

It is important to understand that specificity and sensitivity are calculated within populations where it is already known, if subjects are positive or negative for a condition via use of a gold standard [13]. They indicate how well a test matches a reference standard by distinguishing false negatives, false positives, true positives and true negatives [14]. The purpose of this study was to validate positive contrast radiography for practical use in a clinical scenario where the above conditions may not fully apply, as a synovial fluid sample may not always be obtained. Positive and negative predictive values could therefore provide a more useful measure of test accuracy, as they indicate the probability that a test will give the correct result in a given population [15]. A positive predictive value is defined as the proportion of subjects with a positive test result that actually have a condition and a negative predictive value is the proportion of subjects with a negative test result who do not have the condition [11]. The positive predictive value of positive contrast radiography in our cases was 68.4%. Similar to the calculation of sensitivity, positive contrast radiography performed moderately, below the gold standard set by SFA. However, the negative predictive value of positive contrast radiography was 80.9% and closer to the gold standard with regards to identifying cases that do not have synovial infection. The high negative predictive value also correlates well with the high specificity, as a high specificity means that the test frequently correctly identifies a patient as being negative. The limitation of predictive values as measurements is, that they cannot be directly extrapolated into other populations, as they take into account the prevalence of a condition in the given population. The low positive predictive value in our population could therefore be explained by the fact, that prevalence of actual synovial infection was low (33.3%).

In summary, positive contrast radiography alone had only limited potential for ruling out synovial infection in traumatic wounds, which was reflected by the moderate sensitivity identified. On the other hand, positive contrast radiography had very good ability to confirm synovial infection, as indicated by the high specificity observed. Positive contrast radiography performed at a comparable standard to SFA for identifying synovial infection negative cases (high negative predictive value), but below SFA when identifying synovial infection positive cases (low positive predictive value). The inferior performance in comparison to the gold standard of SFA could additionally be influenced by multiple external factors, such as technical aspects of positive contrast radiography method used, experience and skill of the examiner, as well as type, age and conformation of the traumatic wound.

Conclusions

In agreement with other clinicians, we believe that positive contrast radiography should be performed in horses with traumatic wounds adjacent to synovial cavities to evaluate the need for adequate and timely surgical treatment [9], particularly if no synovial fluid sample can be obtained for laboratory analysis. Positive contrast radiography should be undertaken in combination with other tests, such as arthrocentesis, ultrasonography and aseptic probing for the correct diagnosis to be obtained. This appears most pertinent to horses with a negative positive contrast radiography result, because the low sensitivity of the test creates a potential for false negative results. The results of the present study should be carefully interpreted, taking into consideration that positive contrast radiography may perform differently as a test in another population of horses with different wounds.

Author's declaration of interests

No competing interests have been declared.

Ethical animal research

This retrospective study was approved by the institutional ethical committee of the Royal Veterinary College. Explicit owner informed consent for inclusion of animals in this study was not stated.

Authorship

H. Bryant and D. Bolt contributed to data collection and analysis and writing of the manuscript. J. Dixon and R. Weller contributed to writing of the manuscript.

Manufacturer's address

[a]IBM Corporation, Armonk, New York, USA.

Figure Legends

Fig 1: LM radiographic views of the LF foot in horse with a solar penetration. a) Metal foreign body (nail, black arrow) directing towards the podotrochlear apparatus. b) 19G spinal needle introduced from palmar into the navicular bursa, after the nail has been removed. Sampling of synovial fluid for laboratory analysis should be attempted at this time. c) The navicular bursa has been maximally distended with positive contrast material and no extravasation is identified (positive contrast radiography negative).

References

1. Morton, A.J. (2006) Diagnosis and management of septic arthritis. V*et. Clin. North Am. Equine Pract.* **21**, 627-649.

2. Schneider, R.K., Bramlage, L.R., Moore, R.M., Mecklenburg, L.M., Kohn, C.W. and Gabel, A.A. (1992) A retrospective study of 192 horses affected with septic arthritis/tenosynovitis. *Equine Vet. J.* **24**, 436-442.

3. McIlwraith, C.W., Frisbie, D.D. and Kawcak, C.E. (2012) The horse as a model of naturally occurring osteoarthritis. *Bone and Joint Research* **1**, 297-309.

4. Milner, P.I., Bardell, D.A., Warner, L., Packer, M.J., Senior, J.M., Singer, E.R. and Archer D.C. (2014) Factors associated with survival to hospital discharge following endoscopic treatment for synovial sepsis in 214 horses. *Equine Vet. J.* **46**, 701-705.

5. Summerhays, G.E.S (2000) Treatment of traumatically induced synovial sepsis in horses with gentamicin-impregnated collagen sponges. *Vet. Rec.* **147**, 184-188.

6. Walmsley, J.A., Anderson, G.A., Muurlink, M.A. and Whitton, R.C. (2011) Retrospective investigation of prognostic indicators for adult horses with infection of a synovial structure. *Aust. Vet. J.* **89**, 226-231.

7. McIllwraith, C.W., Frisbie, D.D., Kawcak, C. and Van Weeren, R. (2016) *Joint Disease in the Horse*, 2nd edn, Elsevier, St Louis, Missouri, pp. 91-104.

8. Fiske-Jackson, A.R., Barker, W.H.J., Eliashar, E., Foy, K. and Smith, R.K.W. (2013) The use of intrathecal analgesia and contrast radiography as preoperative diagnostic methods for digital flexor tendon sheath pathology. *Equine Vet. J.* **45**, 36-40.

9. Barker, W.H.J. (2016) Contrast radiography in the equine orthopaedic case. *Equine Vet. Educ.* **28**, 546-549.

10. Gough, M.R., Munroe G.A. and Mayhew G. (2002) Urea as a measure of dilution of equine synovial fluid. *Equine Vet. J.* **34**, 76-79.

11. Parikh, R., Mathai, A., Parikh, S., Chandra Sekhar, G. and Thomas, R. (2008) Understanding and using sensitivity, specificity and predictive values. *Indian Journal of Ophthalmology* **56,** 45-50.

12. Akobeng, A.K. (2006) Understanding diagnostic tests 1: sensitivity, specificity and predictive values. *Foundation Acta Paediatrica* **96**, 338-341.

13. Naeger, D.M., Kohi, M.P., Webb, E.M., Phelps, A., Ordovas, K.G. and Newman, T.B. (2013) Correctly Using Sensitivity, Specificity, and Predictive Values in Clinical Practice: How to Avoid Three Common Pitfalls. *Am. J. Roentgenol.* **200**, 566-570.

14. Oluseyi, A. and Chung, K.C. (2012) Assessing Strength of Evidence in Diagnostic Tests. *Plastic Reconstruction Surgery* **128**, 989-998.

15. Altman, D.G. and Bland, J.M. (1994) Diagnostic tests 2: predictive values. *Br. Med. J.* **309**, 102.

Supporting Information

Supplementary Item 1: Frequency of infected and non-infected synovial structures associated with wounds examined with positive contrast radiography.