—Full Paper—

Incidence of surgical site infection after internal fixation of the first phalangeal bone and the third metacarpal/metatarsal bone fractures in Thoroughbred racehorses

Hiroshi MITA^{1*}, Taisuke KURODA¹, Hidekazu NIWA², Norihisa TAMURA¹, Kentaro FUKUDA¹ and Minoru OHTA¹

¹Clinical Veterinary Medicine Division, Equine Research Institute, Japan Racing Association, Tochigi 329-0412, Japan ²Microbiology Division, Equine Research Institute, Japan Racing Association, Tochigi 329-0412, Japan

Surgical site infection (SSI) is one of the major complications of equine fracture surgery. The purpose of this study was to investigate the incidence of and risk factors for SSI after internal fixation of the first phalangeal bone (P1) and the third metacarpal/metatarsal bone (MC3/MT3) fractures in Thoroughbred racehorses. Between 2011 and 2020, 451 cases underwent surgery with screws or a locking compression plate (LCP) for sagittal fractures of P1 or condylar fractures of MC3/MT3. Overall, 2.9% (13/451) of the cases developed an SSI. The incidence was significantly higher in plate fixation (21.4%) than in screw fixation (2.3%). There was no significant association with other variables, such as sex, age, number of screws, experience of surgeon, or prophylactic antimicrobials. The median duration of hospitalization for screw fixation was 14 days without an SSI and 20 days with an SSI, and those for plate fixation were 26 and 25–88 days, respectively, indicating that the development of SSI prolongs the duration of hospitalization. On the other hand, there were no significant differences in discharge and race resumption rates between cases with and without an SSI. These data indicate that the incidence of SSI in this study was low and that it was higher following plate fixation than screw fixation.

Key words: implant surgery, simple fracture, surgical site infection

Surgical site infection (SSI) is a major complication of equine fracture surgery. It is important to investigate risk factors for SSI and to reduce the incidence, because the development of an SSI decreases the discharge rate [1, 8], extends the duration of hospitalization [1, 4], and increases treatment costs [11, 22, 29]. The incidence of SSI in various orthopedic surgeries in horses has been reported to be 0.2% for arthroscopic removal of carpal chip fractures in Japanese racehorses [19] but to be from 14.2% to 80% in fracture surgeries with implants [1, 8, 13, 17, 18]. There are many risk factors for SSI in each type of surgery, including open fractures [28], sex (mares) [18], open reduction [1, 13], and

©2023 Japanese Society of Equine Science

J. Equine Sci. Vol. 34, No. 3 pp. 61–66, 2023

increased operative time [1, 18].

Prophylactic antimicrobials are generally used in surgery; first-generation cephalosporins reduce the risk of SSI in human orthopedic surgery [23]. A guideline for equine orthopedic surgery recommends prophylactic antimicrobials such as penicillin or gentamicin 1 hr before incision in low-risk surgeries such as elective surgeries without implants and 1 hr before incision and 24-48 hr after surgery in moderate- (≤3 lag screws) to high-risk surgery (all procedures requiring substantial implant materials) [26]. Furthermore, the pharmacokinetics and safety for antimicrobial regional limb perfusion (RLP) have been studied for many kinds of antimicrobials [9, 12, 20, 24], and antimicrobial RLP is sometimes used prophylactically for high-risk surgeries with implants [10]. Nevertheless, there is no clear evidence that this method is prophylactically effective for SSI in equine fracture surgery.

In Japanese racehorses, simple fractures such as condyle fractures of the third metacarpal/metatarsal bone (MC3/MT3) and sagittal fractures of the first phalangeal bone

Received: January 6, 2023

Accepted: April 19, 2023

^{*}Corresponding author. e-mail: Hiroshi_Mita@jra.go.jp

This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (by-nc-nd) License. (CC-BY-NC-ND 4.0: https://creativecommons.org/licenses/ by-nc-nd/4.0/)

(P1) are frequent. The many published epidemiological studies on implant surgery focus on relatively severe fractures and exclude surgery using small-volume implants, as is common in Japan [1, 8]. Moreover, no studies have analyzed only clean, simple fracture surgery, because the analyses include contaminated surgery and severe fractures [18]. To the best of our knowledge, there are no reports of SSI incidence and risk factors specific to surgery with implants for such fractures. In addition, there are no reports of the use of antimicrobial agents to verify the usefulness of prophylactic antimicrobials in racehorse surgery in Japan. Therefore, the purpose of this study was to investigate the incidence and risk factors of SSI after internal fixation of P1 and MC3/MT3 fractures in Thoroughbred racehorse, and to evaluate the use of prophylactic antimicrobial agents and their efficacy.

Materials and Methods

The protocols for the study were reviewed and approved by the Research Committee of Japan Racing Association (JRA; permit number: 2022-3296-04).

Study design

The electronic medical records of all Thoroughbred racehorses that underwent screw or plate surgery for sagittal fractures of P1 or condylar fractures of MC3/MT3 between 2011 and 2020 were reviewed. The records covered treatments performed by veterinarians employed by the Japan Racing Association.

Surgical procedures

Surgeries were performed under general anesthesia or standing sedation with local anesthesia. Surgical sites were shaved with clippers, washed with povidone-iodine scrub, and disinfected with isopropanol and 10% povidone-iodine. An antimicrobial incise drape (Ioban, 3M, Tokyo, Japan) was attached. Screw fixation surgeries used 4.5-mm cortical bone screws. Plate fixation surgeries used a locking compression plate (LCP) with 10 to 13 holes. All implants were inserted by using a minimally invasive technique via a stub incision [13]. The antimicrobial agent used and duration of administration were determined by the surgeon. The frequently used antimicrobial agents were cephalothin (10 g/horse, iv, q 12 hr, Coaxin injection 2 g, Chemix Inc., Yokohama, Japan), amikacin (1.0 g/horse, RLP, amikacin sulfate injection, Nichi-Iko Pharmaceutical Co., Ltd., Toyama, Japan), and kanamycin (5.0 g/horse, im, q 24 hr, kanamycin injection 250, Fujita Pharmaceutical Co., Ltd., Tokyo, Japan). Preoperative systemic or local administration of antimicrobials was performed within 1 hr before incision.

Data collection and variables

Data collected from the medical records comprised signalment, diagnosis, hospital, surgeon's experience, surgery duration, use of prophylactic antimicrobials, duration of antimicrobial use, onset of SSI, bacterial identification, duration of hospitalization, hospital discharge information, and race resumption (defined as participation in at least one race after surgery). SSI was identified according to the criteria of Curtiss *et al.* [8]: in brief, the criteria were a positive bacterial culture from the surgical site or its drainage together with a change in comfort or the development of a fever (>38.6°C) that could not be otherwise explained.

Statistical analysis

Data are presented as medians (interquartile range). Outcome was defined as the development or lack of development of an SSI, and the association of SSI with each variable was tested. We tested the association of SSI with the discharge rate, resumption rate, and number of days in hospital by Fisher's exact test, chi-squared test, or Wilcoxon's rank-sum test and used the Benjamin–Hochberg method for multiple comparisons. Values with a Benjamin–Hochberg-adjusted P<0.05 were considered statistically significant. Statistical analyses were conducted in the JMP v. 16 software (SAS Institute Inc., Cary, NC, USA) or EZR software, which is a version of R Commander modified to add statistical functions frequently used in biostatistics [14].

Results

The number of cases that met the criteria was 451. The median age was 3 (2–3) years. Overall, 2.9% (n=13/451) of the cases developed an SSI. The relationship between each factor and the occurrence of SSI is shown in Table 1. The incidence of SSI was significantly higher in plate fixation cases than in screw fixation cases. There was no significant association with any other variable.

Summary of the surgeries

Surgical time was 55 (40–70) min in screw fixation and 160 (123–191) min in plate fixation. Surgery performed by 33 surgeons. Screw fixation was performed with 2 (2–4) screws, and plate surgery was performed with 1 LCP and 11 (9.75–12) screws. The rate of patient discharge was 98.0% (442/451).

Treatment and prognosis of SSIs

SSIs occurred on postoperative day 7 (4.5–10). Twelve of the thirteen cases had superficial SSIs. They were treated by local irrigation and systemic administration of antimicrobials on the basis of antimicrobial susceptibility testing. The remaining case developed an SSI at the third metatarsal

Variables		SSI (n)	No SSI (n)	Odds ratio	P value
Hospital	Hakodate	0	17		1.00
-	Miho	5	229	Ref.	
	Ritto	8	192	1.90	0.82
Sex	Gelding	0	17		
	Female	1	146	Ref.	
	Male	12	275	6.40	0.21
Age		OR for 1	l-y change	0.89	0.51
Affected bone	First phalanx of hind limb	1	75	Ref.	
	First phalanx of fore limb	3	113	2.05	1.00
	Third metacarpal bone	7	198	2.65	1.00
	Third metatarsal bone	2	55	2.73	1.00
Surgical time	<30 min	0	33		1.00
	31–60 min	5	172	Ref.	
	>60 min	6	132	1.56	0.90
	Not recorded	2	101		
Implant	Screw only	10	427	Ref.	
	Screw and plate	3	11	11.65	< 0.01
Number of screws	1–2	6	224	Ref.	
(only for surgeries using screws)	3–4	1	157	0.24	0.25
	>5	3	43	2.60	0.25
	Not recorded	0	3		
Surgeon's experience	3–5	2	84	Ref.	
(in years)	6–10	5	185	1.49	1.00
	>11	6	169	1.14	1.00
Prophylactic antimicrobials	Kanamycin	0	64		1.00
	Cephalotin	2	144	Ref.	
	Systemic cephalotin and local amikacin	2	99	1.45	1.00
	Local amikacin	4	50	5.76	0.23
	Others*	3	48	4.50	
	None	2	33	4.36	0.37
Anesthesia method	General anesthesia	13	418	-	
	Standing sedation	0	20	-	1.00

Table 1. Association of variables with the development of surgical site infection (SSI)

OR: odds ratio. *Mycillin (combination of penicillin G procaine and streptomycin sulphate), polymyxin, marbofloxacin, or a combination of cephalotin, amikacin, polymyxin B, and kanamycin.

bone plate fixation site on postoperative day 3. It was treated with antimicrobials, and no signs of infection were seen after the removal of the plate 2 months after surgery.

Among the screw fixation cases, there was no significant difference in the discharge rate, with it being 100% (10/10) for those with an SSI and 98.1% (419/427) for those without an SSI. The 8 cases that could not be discharged comprised 4 cases of fatal fracture during recovery from anesthesia or hospitalization, 2 cases of gastrointestinal disease (enteritis and colic), and 2 cases of laminitis. The duration of hospitalization was 20 days (15–33.5) for those with an SSI, significantly longer than the 14 days (13–18) for those without an SSI (P<0.01). There was no significant difference in the race resumption rate, with it being 60% (6/10) in the cases with an SSI and 61.4% (262/427) in those without an SSI.

Among the plate fixation cases, there was no significant difference in the discharge rate, with it being 66.7% (2/3) for those with an SSI and 100% (11/11) for those without an SSI. One case that developed an SSI could not be discharged because of anaphylactic shock. The other two were discharged on days 25 and 88 after surgery. The cases without SSIs were discharged on day 26 (18–44). The race resumption rate was 33.3% (1/3) for those with an SSI and 45.5% (5/11) for those without an SSI, with no significant difference.

Antibacterial administration

The prophylactic antimicrobials and durations (including the operating day) of use were 4 (4–5) days for systemic administration of cephalothin (n=146); 4 (4–5) days for systemic administration of cephalothin plus 1 (1–1) day for regional limb perfusion (RLP) of amikacin (n=101); 3 (2.3–3) days for kanamycin (n=64); and 1 (1–1) day for RLP of amikacin without systemic antimicrobials (n=54). Other prophylactic antimicrobials were administered to 51 cases, and none was administered to 35 cases. The rates of each antimicrobial used are shown in Table 1. In the cases that developed SSI or other complications, antimicrobials other than prophylactics were used.

The choices of these prophylactic antimicrobials were biased according to the type of surgery. In plate surgery, cephalothin plus polymyxin B was administered the most (57%, 8/14, of the cases), followed by cephalothin combined with amikacin RLP (28.6%, 4/14, of the cases). There were no cases in which kanamycin or amikacin was used alone. On the other hand, in screw fixation, there was no significant difference between the number of screws used and kinds of the prophylactic antimicrobial groups (data not shown).

Bacterial isolation

Pathologists tested 5 of the 13 SSI cases for bacteria and detected 11 isolates: methicillin-resistant Staphylococcus aureus (MRSA), 2 isolates; methicillin-sensitive Staphylococcus aureus (MSSA), 1 isolate; Mammaliicoccus sciuri (formerly Staphylococcus sciuri), 1 isolate; Streptococcus equisimilis, 1 isolate; Aerococcus sp., 1 isolate; aerobic Gram-positive rod, 1 isolate; Escherichia coli, 1 isolate; Pseudomonas aeruginosa, 2 isolates; and Elizabethkingia sp., 1 isolate. Multiple species were isolated in 2 of the 5 cases. These isolates (except for MRSA) were susceptible to drugs commonly used in horses. For example, the Gram-positive bacterium was susceptible to cephalothin, and most Gram-negative bacteria were susceptible to gentamicin, amikacin, enrofloxacin, and marbofloxacin. On the other hand, the 2 MRSA isolates were resistant to those antimicrobials but were susceptible to sulfamethoxazoletrimethoprim.

Discussion

Previous studies have not reported the incidence of and risk factors for SSIs in only clean surgery for condyle fractures of MC3/MT3 and sagittal fractures of P1. This study shows that the incidence of SSI in these fractures was 2.9% and that it was higher in plate fixation (3/14=21.4%) than in screw fixation (10/437=2.3%). A previous report indicated that SSIs occurred in 8.1% of cases of clean surgery, 13.3% of cases of screw/wire/plate surgery, and 31% of cases of plate/bone graft surgery [18]. The rate of SSI in various bone surgeries in horses was about 5% for screw fixation and about 16% for LCP [1]. These results cannot be simply compared with our results because those reports include more severe cases than our report, in which the SSI rate was lower. The reason for the lower rate may be that most of the fractures in this study were close fractures that developed from the articular surface, most of the bone fragments did not displace, and a closed technique could be used, which lowers the risk of SSI [1]. We attribute the higher incidence of SSI in plate fixation cases to the greater soft tissue and bone tissue damage associated with plate insertion and the relatively large dead space around the plate. Various reports have shown that operative time is a risk factor for the development of an SSI [1, 8, 13, 18]. However, we found no significant association of operative time or the number of screws with the development of an SSI. Possible reasons for this include the small sample size in this study.

Some reports have indicated that the development of an SSI extended the duration of hospitalization [1, 4] and decreased discharge rates [1, 8]. We too found that SSIs prolonged the duration. On the other hand, we found no significant difference in the discharge and race resumption rates. These results suggest that the prognosis for a superficial SSI after simple fracture surgery is good. We attribute the good discharge outcome to early control of infection by cleaning subcutaneous tissue and administering appropriate antimicrobial agents. However, MRSA prolonged the treatment period, and the affected case was not cured until the implants were removed.

In this patient population, systemic administration of cephalothin was the main choice for the prophylaxis of postoperative infection, followed by the addition or modification of RLP of amikacin. Although not significantly so, the incidence of SSI was lower in cases treated with cephalothin (systemic administration or combined with amikacin) than in those treated with amikacin alone or not treated with antimicrobials. Gram-positive cocci such as staphylococci are frequently isolated in orthopedic SSIs [2, 8], and therefore beta-lactam antibiotics, including penicillin and cephalosporins, are recommended in equine guidelines [26]. Cephalothin has also been reported to be effective for Gram-positive coccal infections in horses at the dose used in this study (22 mg/kg 2 to 3 times daily) [16]. Based on these previous reports and this study, cephalothin may be useful for prophylactic administration. Although beta-lactams are recommended in equine guidelines, there was a group of cases that received kanamycin alone or amikacin alone in this study. The background for use of a single administration of aminoglycoside in this study might have been a period of time when Clostridioides difficile colitis occurred after various surgical procedures (including bone fracture surgery, castration, and laryngoplasty) at this hospital [21]. Since many of those cases were given cephalothin preoperatively, the surgeon may have preferred

to choose kanamycin which was considered as lower risk of antimicrobial-associated diarrhea than cephalosporin as prophylaxis during this period [3, 5]. This temporal selection bias for this antimicrobial ended after hygiene management reduced the cases of *Clostridioides difficile* colitis in this hospital. Although there were no SSIs in the cases that were administered kanamycin in this study, the usefulness of a single aminoglycoside alone is unknown due to the small sample size and the retrospective nature of the study, which is a major limitation of this study. Moreover, there was selection bias due to the surgeon's preference with respect to the choice of antimicrobial agents. Therefore, it is necessary to verify efficacy for prevention of SSIs or side effects such as diarrhea and the risk of bacterial resistance with longterm administration [27] in randomized controlled trials.

The isolates in this study were mainly Gram-positive cocci, and they were consistent with those in previous reports from other countries [1, 8]; however, our isolates included MRSA, which reduced the rate of susceptibility to beta-lactam antibacterials. We found that many infections with bacteria other than MRSA were susceptible to routinely used antimicrobials and were cured early, but MRSA was difficult to treat because of the limited choice of antimicrobials. Intramedullary administration of vancomycin and RLP of imipenem are potentially effective against MRSA in equine lower limbs [15, 25]. Although these therapies offer promise, they should be used cautiously in horses because they are important treatments in humans.

There are several limitations to this study. Most of the SSIs were detected only during hospitalization. Although SSIs can be evaluated on days 6–9 [6] in abdominal surgery in horses, the detection period in orthopedic surgery may be longer. For example, it has been reported that the incidence of SSI in human closed fracture surgery depended on the follow-up period: 40% by 10 days after surgery but 88% by 30 days after surgery [7]. In the present study, some of the horses that developed an SSI after discharge from the hospital were readmitted, but others might have been treated by private veterinarians.

In conclusion, implant surgery for simple fractures of the equine fetlock joint had an overall SSI incidence of 2.9%, with a higher incidence following plate fixation than screw fixation. The prophylactic antimicrobials used varied, and further investigation is needed to verify efficacy.

References

 Ahern, B.J., Richardson, D.W., Boston, R.C., and Schaer, T.P. 2010. Orthopedic infections in equine long bone fractures and arthrodeses treated by internal fixation: 192 cases (1990–2006). *Vet. Surg.* **39**: 588–593. [Medline] [CrossRef]

- Arciola, C.R., Cervellati, M., Pirini, V., Gamberini, S., and Montanaro, L. 2001. Staphylococci in orthopaedic surgical wounds. *New Microbiol.* 24: 365–369. [Medline]
- Mc, B.C., and Gorum, R.S.P. 2010. Antimicrobial associated diarrhoea in the horse. Part 2: which antimicrobials are associated with AAD in the horse? *Equine Vet. Educ.* 22: 43–50. [CrossRef]
- Ban, K.A., Minei, J.P., Laronga, C., Harbrecht, B.G., Jensen, E.H., Fry, D.E., Itani, K.M., Dellinger, E.P., Ko, C.Y., and Duane, T.M. 2017. American college of surgeons and surgical infection society: surgical site infection guidelines, 2016 update. *J. Am. Coll. Surg.* 224: 59–74. [Medline] [CrossRef]
- Barr, B.S., Waldridge, B.M., Morresey, P.R., Reed, S.M., Clark, C., Belgrave, R., Donecker, J.M., and Weigel, D.J. 2013. Antimicrobial-associated diarrhoea in three equine referral practices. *Equine Vet. J.* 45: 154–158. [Medline] [CrossRef]
- Bischofberger, A.S., Brauer, T., Gugelchuk, G., and Klohnen, A. 2010. Difference in incisional complications following exploratory celiotomies using antibacterialcoated suture material for subcutaneous closure: prospective randomised study in 100 horses. *Equine Vet. J.* 42: 304–309. [Medline] [CrossRef]
- Boxma, H., Broekhuizen, T., Patka, P., and Oosting, H. 1996. Randomised controlled trial of single-dose antibiotic prophylaxis in surgical treatment of closed fractures: the Dutch Trauma Trial. *Lancet* 347: 1133–1137. [Medline] [CrossRef]
- Curtiss, A.L., Stefanovski, D., and Richardson, D.W. 2019. Surgical site infection associated with equine orthopedic internal fixation: 155 cases (2008–2016). *Vet. Surg.* 48: 685–693. [Medline] [CrossRef]
- Dahan, R., Oreff, G.L., Tatz, A.J., Raz, T., Britzi, M., and Kelmer, G. 2019. Pharmacokinetics of regional limb perfusion using a combination of amikacin and penicillin in standing horses. *Can. Vet. J.* 60: 294–299. [Medline]
- Daniels, A., Pezzanite, L.M., Griffenhagen, G.M., and Hendrickson, D.A. 2022. Evaluation of factors associated with surgical site infection in equine proximal interphalangeal joint arthrodesis: 54 cases (2010–2019). *Vet. Med. Sci.* 8: 1478–1488. [Medline] [CrossRef]
- Fukuda, H., Sato, D., Iwamoto, T., Yamada, K., and Matsushita, K. 2020. Healthcare resources attributable to methicillin-resistant Staphylococcus aureus orthopedic surgical site infections. *Sci. Rep.* 10: 17059. [Medline] [CrossRef]
- Gustafsson, K., Tatz, A.J., Dahan, R., Abu Ahmad, W., Britzi, M., Sutton, G.A., and Kelmer, G. 2021. Synovial concentration of trimethoprim-sulphadiazine following regional limb perfusion in standing horses. *Animals (Basel)* 11: 11. [Medline]
- 13. James, F.M., and Richardson, D.W. 2006. Minimally invasive plate fixation of lower limb injury in horses: 32

cases (1999–2003). *Equine Vet. J.* **38**: 246–251. [Medline] [CrossRef]

- Kanda, Y. 2013. Investigation of the freely available easyto-use software 'EZR' for medical statistics. *Bone Marrow Transplant.* 48: 452–458. [Medline] [CrossRef]
- Kelmer, G., Tatz, A.J., Kdoshim, E., Britzi, M., and Segev, G. 2017. Evaluation of the pharmacokinetics of imipenem following regional limb perfusion using the saphenous and the cephalic veins in standing horses. *Res. Vet. Sci.* 114: 64–68. [Medline] [CrossRef]
- Kuroda, T., Minamijima, Y., Niwa, H., Tamura, N., Mita, H., Fukuda, K., Kaimachi, M., Suzuki, Y., Enoki, Y., Taguchi, K., Matsumoto, K., Toutain, P.L., Bousquet-Melou, A., and Kasashima, Y. 2021. Rational dosage regimens for cephalothin and cefazolin using pharmacokinetics and pharmacodynamics analysis in healthy horses. *Equine Vet.* J. 53: 1239–1249. [Medline] [CrossRef]
- Levine, D.G., and Richardson, D.W. 2007. Clinical use of the locking compression plate (LCP) in horses: a retrospective study of 31 cases (2004–2006). *Equine Vet. J.* 39: 401–406. [Medline] [CrossRef]
- MacDonald, D.G., Morley, P.S., Bailey, J.V., Barber, S.M., and Fretz, P.B. 1994. An examination of the occurrence of surgical wound infection following equine orthopaedic surgery (1981–1990). *Equine Vet. J.* 26: 323–326. [Medline] [CrossRef]
- Mita, H., Tamura, N., Fukuda, K., Kuroda, T., Kuwano, A., and Sato, F. 2022. Incidence of carpal fractures and risk factors for recurrent fractures after arthroscopic removal of carpal chip fracture fragments in Thoroughbred racehorses. *Vet. Rec.* 190: e1482. [Medline] [CrossRef]
- Mosichuk, A.P., Smith, J.S., Tatarniuk, D.M., Troy, J.R., and Kreuder, A.J. 2021. Meropenem administered via intravenous regional limb perfusion for orthopedic sepsis in horses: a clinical retrospective study. *Front. Vet. Sci.* 8: 629627. [Medline] [CrossRef]
- Nomura, M., Kuroda, T., Tamura, N., Muranaka, M., and Niwa, H. 2020. Mortality, clinical findings, predisposing factors and treatment of *Clostridioides difficile* colitis in Japanese thoroughbred racehorses. *Vet. Rec.* 187: e14.

[Medline] [CrossRef]

- O'Connor, O., Thahir, A., and Krkovic, M. 2022. How much does an infected fracture cost? *Arch. Bone Jt. Surg.* 10: 135–140. [Medline]
- Rubinstein, E., Findler, G., Amit, P., and Shaked, I. 1994. Perioperative prophylactic cephazolin in spinal surgery. A double-blind placebo-controlled trial. *J. Bone Joint Surg. Br.* 76: 99–102. [Medline] [CrossRef]
- Rubio-Martínez, L.M., López-Sanromán, J., Cruz, A.M., Santos, M., Andrés, M.S., and Román, F.S. 2005. Evaluation of safety and pharmacokinetics of vancomycin after intravenous regional limb perfusion in horses. *Am. J. Vet. Res.* 66: 2107–2113. [Medline] [CrossRef]
- Rubio-Martínez, L.M., López-Sanromán, J., Cruz, A.M., Tendillo, F., Rioja, E., and San Román, F. 2006. Evaluation of safety and pharmacokinetics of vancomycin after intraosseous regional limb perfusion and comparison of results with those obtained after intravenous regional limb perfusion in horses. *Am. J. Vet. Res.* 67: 1701–1707. [Medline] [CrossRef]
- Santschi, E.M. 2006. Prevention of postoperative infections in horses. *Vet. Clin. North Am. Equine Pract.* 22: 323–334, viii viii. [Medline] [CrossRef]
- So, J.P., Aleem, I.S., Tsang, D.S., Matlow, A.G., Wright, J.G., SickKids Surgical Site Infection Task Force. 2015. Increasing compliance with an antibiotic prophylaxis guideline to prevent pediatric surgical site infection: before and after study. *Ann. Surg.* 262: 403–408. [Medline] [CrossRef]
- Stewart, S., Richardson, D., Boston, R., and Schaer, T.P. 2015. Risk factors associated with survival to hospital discharge of 54 horses with fractures of the radius. *Vet. Surg.* 44: 1036–1041. [CrossRef]
- Zimlichman, E., Henderson, D., Tamir, O., Franz, C., Song, P., Yamin, C.K., Keohane, C., Denham, C.R., and Bates, D.W. 2013. Health care-associated infections: a meta-analysis of costs and financial impact on the US health care system. *JAMA Intern. Med.* 173: 2039–2046. [Medline] [CrossRef]